JANUARY, 1949

# The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

## SYMPOSIUM ON GASTRODUODENAL ULCER

Treatment With Protein Hydrolysate and Aluminum Hydroxide

Treatment of Gastric, Duodenal or Jejunal Peptic Ulcer

Surgical Therapy in Gastroduodenal Ulcer

Differential Diagnosis in Gastric Ulcer

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*Fourteenth Annual Convention*

*Boston, Mass., 24, 25, 26 October 1949*

VOLUME 16 NUMBER 1

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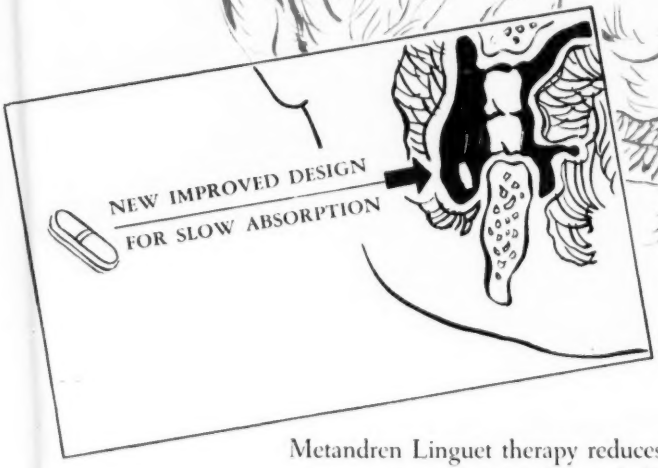


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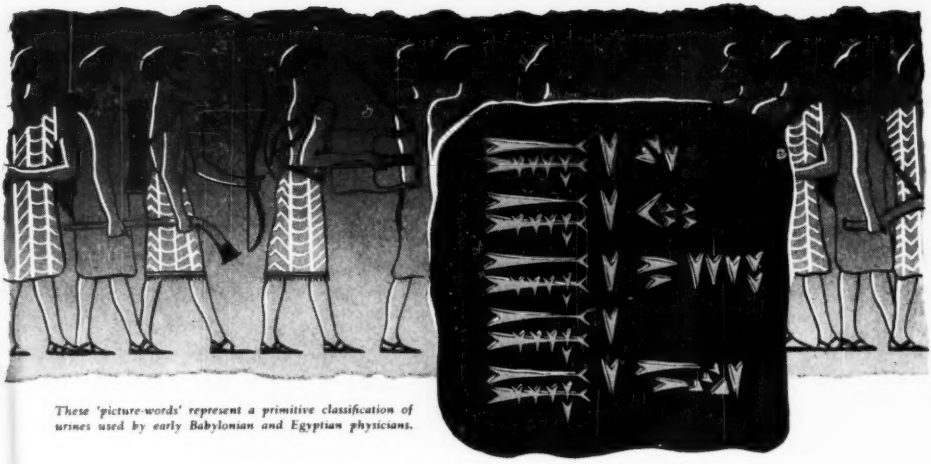

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*The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada*

VOLUME 16 JANUARY, 1949 NUMBER 1

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# The Review of Gastroenterology

OFFICIAL PUBLICATION

*of the*

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

1819 Broadway, New York 23, N. Y.

Editorial Office, 146 Central Park West, New York 23, N. Y.

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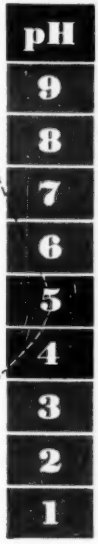


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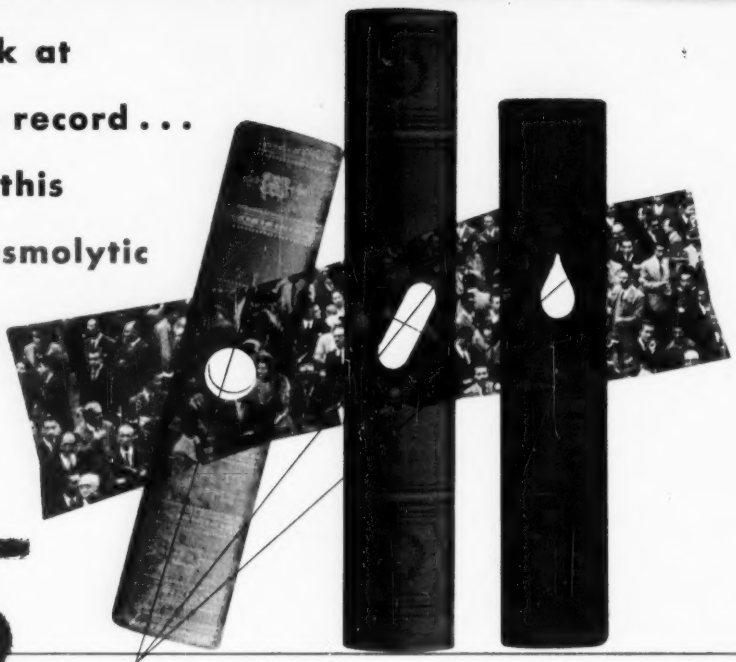

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1. Kilstein, R. I.: Rev. Gastroenterol., 14:171, 1947.
2. Morrissey, J. H.: J. Urol., 57:635, 1947.
3. Ricci, J. V.: in The City Hospital Year Book, 1946, New York, 1947.


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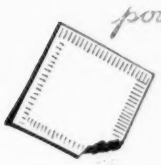

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[1] Weiss, J.: Review of Gastroenterology, Nov., 1948

[2] Kraemer, M.: Conn. State Med. Journ., 12:305, April, 1948

[3] Pfeiffer, C. J., & Spears, M. M.: Gastroent., 8:191 Feb., 1947

[4] Kraemer, M.: Postgrad. Med., 2:431, Dec., 1947

[5] Martin, G. J.: Gastroent., 6:315, April, 1946


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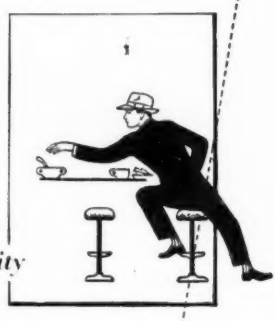

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Volume 16 JANUARY, 1949 Number 1

# SYMPOSIUM ON GASTRODUODENAL ULCER

## THE DIFFERENTIAL DIAGNOSIS IN GASTRIC ULCER*

ARTHUR W. ALLEN, M.D.†

Boston, Mass.

Ulcerative lesions of the duodenum are so rarely associated with malignancy that one need not seriously consider this possibility. Duodenal ulcer occurs in the practice of most clinicians about ten times as often as gastric ulcer. Hiatus hernia, ulcer of the lower esophagus, gastric ulcer, gastritis, duodenitis and duodenal ulcer all give symptoms that are much alike. Also, the same conservative regimen of bland food and antacids has a tendency to ameliorate the discomforts common to all of these. Distinction may be suspected from the symptoms and the physical signs. A correct diagnosis however usually follows more specific studies, especially with the fluoroscope and the gastroscope.

Because gastric ulceration must be treated with more certainty than the other lesions mentioned above, it is necessary to prove or disprove this possibility in all cases. It is not sufficient to entertain a supposition that if the symptoms are improved by diet and alkalis, no further immediate investigation is necessary. For this reason, every doctor should lend his influence towards outlawing the insidious advertising in the press and on the radio regarding the remedies purporting to relieve acid indigestion. It is my belief that many patients with inoperable cancer of the stomach are seen because these antacid proprietary drugs do give temporary relief in the early stages of this dreadful malady. It also behooves us to continuously exhort our colleagues to recognize the danger of these possibilities. Certainly a physician who fails to study his patients thoroughly at the earliest possible moment is derelict in his duty.

Since gastric ulcer is so much less common than duodenal ulcer, a practitioner may go some years without meeting the seriousness of this problem in a graphic manner. One wonders why this is true when there are known to be about 40,000 deaths from cancer of the stomach in the United States each year. The insidious manner in which gastric cancer develops in so many cases is probably the reason

*Read before the Thirteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 7, 8, 9, 10 June 1948.

†Consultant in Surgery, Massachusetts General Hospital, Boston. President, American College of Surgeons.

most cases of carcinoma of the stomach seen in the Massachusetts General Hospital have not consulted a physician until shortly before entry. Symptoms have averaged about six months in duration in these patients. Unfortunately, most of them have had little or no pain and have sought advice finally for weight loss and anorexia.

There are however a considerable number of these advanced lesions that give a history of early symptoms so like those of benign ulceration that one must continuously keep this possibility in mind. It is this group of patients that can be sorted out early in the process and treated radically with hope of cure. Until we accept this fact, we are wasting our best chance to improve the salvage rate in cancer of the stomach. In the last decade analysed at the Massachusetts General Hospital (Welch and Allen[1]) the five-year survivals had risen to 7 per cent of all cases. The resectability had risen to 50 per cent and the operative mortality, in resection for cure, had fallen to 3 per cent. It is out belief that the operability and the cure-rate can be definitely improved if we will take a sound viewpoint on gastric ulcer.

Immediately it will be assumed that we are implying that gastric ulcer may change from a benign to a malignant process. This impression we hasten to correct, since we believe that most gastric cancers begin as such, while there is only an occasional case that appears to have been benign in its earlier phase. It is true that serial sections of a gastric ulcerative lesion may show malignancy in one portion, while the remainder has the characteristic appearance of benign ulcer. Even this does not prove that the ulcer was wholly benign at one time. It seems to us that we should consider all the evidence regarding gastric ulcer and aim our therapeutic endeavors at this problem on a rational basis. It is with these possibilities in mind that I will proceed with a discussion of this subject as a whole.

In a study of the final diagnosis in a group of gastric ulcer patients coming to the Massachusetts General Hospital in a ten-year period, we brought to light some interesting facts[2]. With the clinical evidence supported by roentgenograms, gastroscopies and the gross appearance of the lesion on the operating table, 14 per cent of the cases thought to be benign proved, on pathologic study, to be cancer. In this group of borderline cases, there were some opinions that were doubtful and a few who felt that malignacy could not be ruled out. Reports have followed from other clinics[3, 4] bearing out our own failures with ratios of about 10 per cent errors in diagnosis. On the black side of the ledger, we found that 5 per cent of the patients diagnosed preoperatively as gastric cancer proved to have benign ulcer. The net result of these studies led us to believe that we should be very cautious in advising conservative treatment for many of our gastric ulcer patients. We carefully analysed all the data concerning this group of patients. This was helpful to some extent in the differential diagnosis and will be repeated here.

*The location of the lesion* proved to be of some help since it appeared that nearly all of the ulcerations on the greater curvature of the stomach were malignant. The immediate 2 cm. of the prepyloric region was a danger zone, and in our group proved to be malignant in 65 per cent of the cases. It is believed that this percent-

age may have been reduced considerably since our study was made but, as yet, we cannot be sure of this opinion. Twenty per cent of the ulcers on the anterior or the posterior wall of the stomach proved to be cancer. Ulcers on the lesser curvature and those in the pylorus itself were malignant in 10 per cent of the cases. This may be misleading since one-half of all our gastric ulcerations were found on the lesser curvature and it was in this location that the majority of our errors in diagnosis were made.

*The size of the ulcer* proved to be of some help in making a correct diagnosis. In general, the smaller the ulcer the more apt it was to be benign. The benign ulcers in the group averaged 1.5 cm. in diameter while those that proved to be cancer averaged 2.3 cm. in diameter. This is not a reliable sign since we have seen cancer in very small ulcerations in the prepyloric region and have performed total gastrectomy for enormous ulcerative lesions having the gross appearance of very unfavorable carcinoma only to find that the entire lesion was benign. There is however enough evidence obtained from the size of the lesion to give some help in the proper management of the case.

*The age of the patient and the duration of symptoms* proved of tremendous value in the differential diagnosis. It was found that in patients under forty-five, benign ulcers were much more common than in those beyond this age. It was also obvious that duration of symptoms in the older-age group was very important. In patients of over 45 years of age whose symptoms had existed for five or more years, there was an 80 per cent chance that the lesion was benign. On the other hand, if the duration of symptoms was less than one year in this age-group, benign ulcer was found in only 20 per cent of the cases. This leads us to stress the importance of the short history in these patients of middle age. Ogilvie[5] puts it very well when he states that all restaurants should be required to display a sign "*that indigestion does not begin at forty*". Certainly all of us have had the experience of having a man tell us that up to 6 weeks ago he could eat anything without harm and with good appetite but now he can eat nothing that agrees with him or that is appetizing. It is this type of patient who must be so strongly suspected of having cancer of the stomach and no time must be wasted in obtaining a complete and thorough investigation. If the surgeon could get the patient within 2 instead of 6 months from the first warning of cancer of the stomach, the operability would rise to 75 per cent and the cure-rate to 40 per cent of those resectable.

*Gastric acidity* studies were not helpful in making the differential diagnosis in borderline cases. It was found that 60 per cent of the patients with proved cancer of the stomach had achlorhydria. Therefore, as previously noted, an ulcerative lesion in a patient without hydrochloric acid must be assumed to have malignancy. In the borderline group however, we found that the acid levels were just as high in those who proved to have cancer as they were in those whose lesions proved to be benign. This, we believe, is an important finding and warns us again that early malignant ulcerations may masquerade as benign lesions. We are sure that too much confidence has been placed on gastric acidity with the supposition

that this is evidence of a benign ulcer. We should not make any concession except in the lesion associated with achlorhydria.

*Failures in Conservative Management of Gastric Ulcer*:—I am aware that many gastroenterologists, and certainly the majority of general practitioners, feel that gastric ulcer can be treated with equal success as duodenal ulcer. I personally cannot statistically prove that this is true or false. Reports[3] have appeared in the literature to support the thesis that gastric ulcer is unsatisfactorily managed conservatively in approximately 50 per cent of the cases. We believe that 80 per cent of patients with duodenal ulcer can be treated without surgical interference. It appears to us that, aside from the influence of our findings with errors in diagnosis of gastric ulcer, more of them are referred for surgery than formerly, many because of persistent or recurrent symptoms. It is possible that we cannot properly evaluate the reasons for the more radical attitude in recent years. A further study of this problem will be made in our clinic.

*The relative safety of surgery in gastric ulcer* as compared to duodenal ulcer must be taken into consideration. The normal duodenum offers no problem to the surgeon in gastrectomy for gastric ulcer. This one fact reduces the risk of the operation by at least 50 per cent. Doubtless, this has played a role in the swing towards more radical measures in the treatment of this lesion.

Of the three reasons for treating gastric ulcer surgically, we are sure that the inability by our present methods of investigation to determine the exact nature of the lesion is the most important. A radical attitude towards gastric ulcer will save many lives from cancer of the stomach. This alone seems to me to warrant the assumption that gastric ulcer is primarily a surgical problem. If such an attitude is generally supported, then the cases will be followed more closely and with proper evidence more of these patients will be operated upon in a curable phase of cancer. To be sure, many who do not have cancer will have radical treatment. It is possible if not probable that the net gain even in benign lesions warrants surgical treatment.

It is my belief that:

1. Gastric ulcer is primarily a surgical lesion.

2. Gastric ulcer cannot be differentiated from early cancer of the stomach in a large percentage of cases.

3. The results of surgical treatment in benign gastric ulcer may be better than conservative measures.

4. Surgery should consist in a resection of the distal stomach including the ulcerative lesion and all of the antral segment. This means a high resection on the lesser curvature.

5. Vagus nerve resection has no place in the treatment of gastric ulcer because even frozen section studies cannot rule out areas of malignancy. It is unnecessary to treat gastric ulcer with vagus resection and subtotal gastrectomy because anastomotic ulcer never follows adequate resection in gastric ulcer.

6. Small ulcers in young patients can be treated conservatively. These patients must be carefully followed. *Persistence* of ulceration or apparent recurrence should be looked upon with suspicion.

7. Hospital treatment will lead to a better evaluation of the problems than will ambulatory management.

8. Gastric ulcerations submitted to surgery must be treated as early cancer in all doubtful cases. This means a complete nodal dissection including the great omentum.

9. By this attitude, the cure-rate in gastric cancer can be greatly improved.

10. It might be well to eliminate the term "peptic ulcer" from our nomenclature. Because duodenal ulcer, which is always benign, is so much more common than gastric ulcer, there is still confusion in the minds of the laity and the profession regarding the potentialities of gastric ulceration.

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# THE TREATMENT OF GASTRIC, DUODENAL OR JEJUNAL PEPTIC ULCER*

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For several weeks the necessity of writing something to be presented at this symposium dealing with the therapy of peptic ulcer has weighed heavily upon me. Each morning, while visiting an unusually large number of patients who had been hospitalized for the treatment of this disease, I have attempted to make an orderly summary of what constitutes the fundamental principles involved in treating benign peptic lesions of the stomach, duodenum or jejunum. I must confess that my efforts have brought forth no readily applicable formula which can be employed universally in the intelligent treatment of this disease. It is my opinion that no definite standardization of regimens, whether surgical or medical, for the treatment of all peptic ulcers has been accomplished, and I do not expect that one ever will be. It is indeed debatable whether one should consider peptic ulcer as a specific single disease entity, although there is an element of distinctness about it in so far as it represents a form of dissolution of tissue that occurs in the presence and in consequence of the eroding action of acid gastric juice. It is the local manifestation of a disturbance resulting in circumscribed disintegration of gastric duodenal or jejunal tissues. This disturbance in turn is affected by various systemic causes. It is a disturbance of such varied histopathologic features and the important etiologic factors are so variable that the treatment of the condition will remain a specific problem in each case. Peptic ulcer is not due to a single etiologic factor in a patient of a particular constitutional type. There is no specific factor by which this type of ulcer is produced. The ulcer does not develop because acid of a definite concentration impinges on tissues which have a definite resistance.

In order to treat peptic ulcer effectively, one must therefore turn his perspective from the consideration of the general causes of ulcer and its therapy to the specific causes and their eradication. Each ulcer must be treated in the light of its own pathologic state. A determined plan should be made to control or eradicate the important causes in an individual case.

To treat peptic ulcer symptomatically is the equivalent to the application of tape to a leaking pipe. Nothing lasting is accomplished by such a procedure. There is a tendency to treat the single exacerbation of ulcer as though it were a malady in itself when in reality it constitutes merely a single breakdown in the cycle of the disease. One successful stand against the mechanisms responsible for ulceration does not as a rule end the contending play of forces responsible for the lesion. Reactivation of the ulcer usually remains an active threat particularly in cases in which there is a persistent psychologic undercurrent which readily gets out of

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control and sets in motion the eroding mechanism. Treatment must therefore include some consideration of ways and means of keeping dormant those forces which may be difficult to control when they are stimulated into activity.

## Requirements for Planning a Successful Ulcer Regimen

If the symptoms are severe or if complications are present, treatment may have to be started immediately. Subsequent therapy should be governed by information that is gained by a careful study of the patient. There are two important requisites for planning the treatment of peptic ulcer. These are: (1) evaluation of the etiologic factors in an individual case, and (2) accurate diagnosis.

*Evaluation of the Etiologic Factors in an Individual Case*:—To anyone who sees patients with peptic ulcer daily, it soon becomes evident that the occurrence of this ulcer is not limited to patients of a certain type, age or sex. It is not a seasonal disease. One cannot hope to discover a single causative factor in a certain constitutional type of patient. The architectural designs of ulcer development, however, and the tools utilized in the formation of an ulcer are strikingly similar although the factors which influence them may be quite different in various instances. Successful treatment of ulcer must take into consideration the etiologic factors which are important in all cases of peptic ulcer and those which seem to be particularly important in an individual case.

*Acid Aggression or Erosion*:—There is only one common denominator which is consistently and universally applicable to all peptic lesions; that is, they occur only in tissues bathed by the acid gastric juice. I never have seen a peptic ulcer develop in the absence of hydrochloric acid. Physiologists have definitely established that the erosion factor responsible for peptic ulceration is inherent in the acid-pepsin component of the gastric juice. They have, furthermore, convincingly demonstrated that the erosion mechanism is increased by a greater concentration of acid and perhaps by an increase of peptic activity as well. Ivy and his associates as well as Sandweiss and his associates have demonstrated the presence of the secretory-inhibiting hormones, chalone, enterogastrone and urogastrone. There has been some speculation that ulcer might be the result of a deficiency of these substances.

*Mechanical Trauma*:—One other extremely important cause of erosion, which is often overlooked and which seems important in the formation of duodenal and anastomotic ulcers, and probably also in the formation of gastric ulcers has been pointed out by Mann and Bollman and also by Harper. I refer to the mechanical impingement of the acid gastric contents which determines the site of the development of peptic ulcers in animals. As the garden hose digs a hole where the stream of water incessantly strikes the lawn, so the site where the acid contents impinge on the mucous membranes determines the site at which the ulceration usually will occur. Furthermore, the force of this impinging stream may well determine not only where an ulcer may develop but whether an ulcer actually will develop. Aschoff also suggested that mechanical factors are of importance in cases in which ulcers occur in the stomach; he assumed that such ulcers occur at sites

most exposed to traumatization by acid and gastric contents, that is, along the lesser curvature on the socalled "magenstrasse".

*Resistance of Local Tissues*:—So long as tissues maintain their normal mechanisms of defense they can adequately resist the eroding action of the gastric chyme. Gastroduodenal tissues seem to be endowed by nature with several lines of defense which are singly or in combination utilizable in protecting them against the erosive action of the gastric juice. The front line of defense seems to be in the gastroduodenal cells themselves. The neutralizing effect of alkaline blood in mucosal capillaries, the protective action of gastric or duodenal mucus and perhaps also the presence of antipepsin in the mucosa or of an antiulcer or acid-retarding or acid-regulating factor possessed by enterogastrone or urogastrone, all have been considered as possible explanations of this obvious effect. There is an appreciable difference in the resistance of mucous membranes in different sites to the eroding action of the acid gastric juice. The mucous membrane of the fundus is the most resistant and in order of their diminishing resistance are the mucous membranes of the lesser curvature near the pylorus, the pylorus, duodenum, jejunum and ileum.

The various intrinsic and extrinsic secretions of the duodenum seem to have a protecting influence upon its mucosal surface. Unquestionably, one of the important causes of cellular dissolution which results in peptic ulcer is the exhaustion of the intrinsic and extrinsic cellular defense. If normal tissues can disintegrate under the prolonged bombarding influence of a highly aggressive chyme, it is not difficult to assume increased liability to ulceration in tissues deficient in the capabilities of defense. Disturbances which locally diminish the resistance of the tissues must be important in preparing the soil so that chronic ulcer can be implanted. There are numerous ways in which this can be accomplished; among them are vascular diseases, nutritional disturbances, shallow erosions associated with systemic diseases, septic emboli, foreign bodies and roughage in food. Gastric ulcer occurring at the point of maximal mucosal irritation in conjunction with diaphragmatic hernia would be a further illustration of local insult to tissues which may cause ulcer or keep it from healing. Peptic ulcer is in all probability the result of the interaction of acid aggression or erosion, mechanical trauma and a decreased resistance of local tissues, although each is of varying significance in different cases, and it is probable that even in the same case first one factor and then another may assume the position of major importance.

It is impossible to clarify any of the confusing problems referable to the production of peptic ulcer in man unless one assumes that in spite of the fact that the pathologic result is the same, the instruments, that is, the acid factor, the mechanical factor and the tissue factor, which fabricate the lesion are the same, yet the systemic or the constitutional diathesis which motivates them and influences them may be entirely different and hence will require specific consideration.

*Infection*:—The origin and reactivation of certain ulcers are related to intercurrent infection, acute tonsillitis, sinusitis, enteritis, acute appendicitis or chole-

cystitis. Gastric ulcer is not infrequently found in old people with badly infected teeth, the removal of which facilitates the healing of such lesions.

*Nutritional Disturbances*:—I have reported cases in which vitamin deficiency and malnutrition seemed instrumental in influencing the cause or the course of peptic ulcer. Nissen, Harris, Abbase, Yudkin and Kelly have reported similar cases. Hingston attributed the great number of peptic ulcers among the natives of southern India to the fact that the diets of these people are regularly high in carbohydrates and deficient in proteins.

*Abnormal Tissues*:—Ulcers of this type are associated with foreign bodies, such as bezoars, or with diaphragmatic hernias. In all probability, the traumatizing effect of food on the walls of the stomach is of some importance, in certain instances, in the formation of gastric ulcer. Gastritis or duodenitis may prepare the tissue for the development of ulcer.

*Chemical Factors*:—Gastric acid impinged on tissues not accustomed to receive it is likely to cause ulceration in such tissues. Ulcers that are caused in this manner are peptic ulcers associated with heterotopic gastric tissue in Meckel's diverticulum, gastroiliac ulcers and gastrojejunal ulcers. Even tissues normally accustomed to the bathing effect of the chyme will succumb if required to withstand increased erosion without cyclic retardation of secretory rates. The chemical factor probably is an important one in the cause of most ulcers. The lesions considered in this category are directly related to this factor and are not caused by supervenient constitutional diathesis.

*Constitutional Diathesis*:—By far the largest number of peptic ulcers are attributable to a constitutional diathesis. The four types of ulcer which have just been described are related to "systemic" factors, that is, mechanisms through which general or more localized disease entities as well as anomalous physiologic aberrations affect the vital function of the ulcer-bearing tissues of the gastrointestinal tract. The recognition of these factors is of obvious importance when treatment is advised. Under "constitutional diathesis" I shall consider those characteristics peculiarly inherent in the structure of the physical and mental component of the patient which predispose him to the causation or the reactivation of peptic ulcer and which affect the life cycle of the ulcer generally. Constitutional diathesis may be divided into three components; namely, anatomic, physiologic and psychoneurogenic.

The anatomic component includes certain anthropometric relationships which lead to the presumption of an "ulcer constitution". Hurst and Stewart postulated that a person with a short stomach associated with active peristalsis and rapid evacuation is predisposed to the development of duodenal ulcer, whereas a person with a long stomach, if exposed to the exciting causes of ulceration, is likely to have a gastric ulcer rather than a duodenal ulcer. Some authors have described a vasoneurotic diathesis which is assumed to be related to a congenital or acquired disharmony of the structures and to the function of the peripheral blood vessels.

The Physiologic Component includes unusually rapid and persistent responsiveness of the gastric glands to secretory stimuli. The spastic mechanism inherent in gastric or duodenal musculature seems to be on a similar hair-trigger level. The hyperacidity and the hyperspasticity probably represent the active tools of aggression in the formation of a peptic ulcer. They are tangible characteristics of an ulcer diathesis.

The Psychoneurogenic Component represents the "vis a tergo", the impelling force, which activates the constitutional diathesis. The alternate overflow or control of this force upon the physiologic mechanisms just mentioned could easily be one of the determinants resulting in activity or quiescence of a peptic ulcer. Much has been written regarding the nervous and mental pattern of the patient in whom a peptic ulcer is especially likely to develop. Time prohibits more than the cursory comment that such lesions seem to be found most frequently in the ambitious, tense, high-strung, sensitive person who is given to periods of great worry and concern over the actual or alleged frustrations of life. The time of origin of ulceration or period of recurrence often corresponds accurately with the time when such patients are nervously fatigued or are in the midst of a dilemma which defies successful solution. The recognition of these factors is of great importance in the etiologic consideration of a peptic ulcer in an individual case and in the planning of successful treatment.

*Accurate Diagnosis*:—The treatment of peptic ulcer is greatly facilitated if accurate knowledge regarding its position and pathologic state is available. The first essential in the evaluation of the patient's symptoms is to be certain that those which suggest the presence of a peptic ulcer actually are due to such a lesion. Data available from a carefully taken history must be correlated with information obtained by gastric aspiration, by roentgenologic examination and, in certain instances, by direct inspection of tissues by gastroscopy. It also is important to remember that a duodenal deformity as demonstrated by roentgenologic examination is not sufficient evidence to warrant a presumptive diagnosis of an active duodenal ulcer. To institute an ulcer regimen for the cure of indigestion in the presence of a duodenal scar will be a waste of time if the indigestion was not caused by an active peptic lesion in the duodenum. A careful evaluation of symptoms and laboratory data will prevent such an error. A review of a series of cases of peptic ulcer in which the patients were observed at the Mayo Clinic has disclosed the following facts regarding the association of peptic ulcers. Of a group of patients who had a duodenal ulcer, 6 per cent also had a gastric ulcer. Of a group of patients who had a gastric ulcer, 5.2 per cent also had a duodenal ulcer. In 4 per cent of a series of cases of gastric ulcer, multiple ulcers were present in the stomach. It is of great importance in planning treatment to determine whether multiple ulcers are present.

A complete diagnosis is necessary before ulcer therapy is started. Suggestions of associated disease involving the gallbladder, pancreas, colon or urinary tract must be carefully considered and suitable tests must be applied to prove or disprove their presence. It is also of obvious importance to have accurate knowledge regard-

ing the patients cardiorenal or nutritional status, and to know whether the patient has any infection which might influence the efficacy of ulcer therapy.

No final decision should be made regarding the treatment of any peptic lesion without accurate knowledge regarding complications and the pathologic state of the ulcer in an individual case. It seldom is difficult to ascertain if hemorrhage has occurred. If the patient has vomited blood, this fact will usually be included among the symptoms mentioned by the patient, even if the amount of blood in the vomitus was trivial. The occurrence of tarry stools or of blood in aspirated gastric contents, or the presence of an otherwise unexplainable anemia may further attest to the fact that the ulcer has bled.

In cases of the obstructive type of peptic ulcer, the clinical history usually will reveal whether there is any deficiency in the emptying of the stomach. In cases of this type of ulcer, a retention type of vomiting occurs, aspiration of the gastric contents will disclose the presence of a large amount of residue and roentgenologic examination will reveal defective emptying of the stomach. It then is important to determine if the defective emptying is due to inflammation, to cicatrization or to pyloric spasm. The obstruction resulting from inflammatory reactions usually occurs as one of the manifestations and during the course of a severe exacerbation of peptic ulcer. This happens most frequently in cases of subacute duodenal ulcer, less frequently in cases of anastomotic ulcer, and seldom in cases of gastric ulcer. After the acuteness of the attack subsides, the retention gradually disappears. During the attack, roentgen examination will show defective emptying but normal function of the gastric musculature. After the attack, the stomach will be found to empty normally. In cases of cicatricial obstruction, there is persisting or frequently recurring evidence of gastric stasis. Appetite is poor and there is loss of weight and strength. Dehydration and anemia may develop. Gastric aspiration repeatedly will produce increased amounts of residue, and roentgenologic examination, in addition to demonstrating defective gastric emptying, may disclose a dilated organ and evidence of some muscular atony. Gastric stasis may be the result of pyloric dysfunction. This may occur in cases in which a gastric or duodenal ulcer is situated some distance from the pyloric sphincter. In such cases, the pylorus is unusually spastic and thus prevents normal emptying of the stomach. The clock-like precision of the ulcer syndrome becomes distorted. The patient belches a great deal and there is considerable gaseous distention. Small amounts of sour gastric residue, including food particles, are regurgitated. Gastric aspiration at such times may reveal the presence of 400 to 500 cc. or more of residue. On the next day, there may be no sign of pyloric obstruction and a motor meal usually will fail to disclose an abnormal amount of retained material. These episodes of retention are not necessarily associated with an exacerbation of symptoms of an active ulcer. There frequently is no roentgenologic evidence of defective gastric emptying. Pyloric dysfunction due to spasm is not a serious complication. It should not be confused with organic obstruction.

Accurate knowledge regarding the perforating characteristics of a peptic ulcer in an individual case is of crucial importance in the proper planning of the treat-

ment. Acute free perforation is usually recognized with ease. Occasionally, the advancing erosion succeeds in punching a small hole through the last restraining coat of the viscus. In rare instances, no free flow of visceral content occurs into the peritoneal cavity. This has been designated "subacute visceral perforation". Whereas acute free perforation often occurs in cases of acute peptic ulcer, subacute perforation develops almost exclusively in cases of chronic peptic ulcer. Ordinarily, the symptoms of this complication are similar to those caused by acute perforation except that the pain is less acute and widespread and there are no systemic reactions such as those caused by general peritonitis. A severe pain usually develops after intensified symptoms of ulcer have been present for one or two days. Marked tenderness and localized muscle rigidity develop around the site of the perforation. Movement, jarring or touching this region causes intense pain. Frequently, an inflammatory mass develops. This complication usually is not difficult to recognize.

Failure to recognize the signs of chronic perforation is one of the most frequent causes of disappointment in the therapy of peptic ulcer. It is my opinion that peptic ulcer is productive of five distinct syndromes, each of which is dependent on a certain pathologic state. Careful evaluation of available data usually makes it possible to recognize these syndromes; it greatly increases the accuracy in diagnosis and consequently simplifies the proper choice of treatment. These five syndromes are as follows: (1) visceral ulcer syndrome without referred pain, (2) visceral ulcer syndrome with referred pain, (3) perforating ulcer syndrome with admixture of visceral and somatic syndromes, (4) perforating ulcer syndrome with a somatic syndrome replacing the visceral syndrome and (5) phrenic peptic ulcer syndrome.

Time does not permit a detailed consideration of the anatomic and physiologic principles involved in the production of these syndromes. For several years I have used this classification and I have found that it has been accurate in more than 90 per cent of cases in which an exploratory laparotomy was performed subsequently.

*Visceral Ulcer Syndrome without Referred Pain*:—In this syndrome, an ulcer confined to the visceral wall sets up pain impulses along the afferent sensory fibres mainly or exclusively by the splanchnic pathway. This syndrome includes the symptoms which Moynihan said would warrant the diagnosis of a peptic ulcer over the telephone. This is a well-organized syndrome which follows a cyclic pattern. The distress is situated in the epigastrium. It rarely is very severe, occurs several hours after meals and occasionally awakens the patient at night. The pain is not projected. It is dissipated promptly by food or an alkali. The symptoms disappear in a short time and are followed by a prolonged period of freedom. This type of syndrome is usually indicative of an uncomplicated peptic ulcer. The pain impulses are gathered solely from the visceral wall.

*Visceral Ulcer Syndrome with Referred Pain*:—This syndrome is similar to the one just described except that the symptoms may be more severe and when the pain reaches its maximal intensity it may temporarily extend to other regions. In cases of duodenal ulcer the extension of pain is toward the right costal

margin; in cases of gastric ulcer it is toward the margins of the left ribs, and in cases of anastomotic ulcer it is in the umbilical region. I have found that these symptoms are usually indicative of a large ulcer or multiple ulcers with localized inflammatory reaction surrounding the lesions. The entire process, however, is limited to the visceral wall.

*Perforating Peptic Ulcer Syndrome with Admixture of Visceral and Somatic Syndromes*:—When the ulcer extends by means of penetration or perforation and invades somatic structures surrounding the viscus primarily involved, it generally maintains some of its usual characteristics but a new syndrome will develop. This is not a hybrid syndrome or one which is irregular or adventitious. The structures involved in the penetrating process are supplied by nerves, some of which in all probability relay their impulses through the spinal nerves to the spinal cord. The somatic tissues interpret these reactions thrust upon them by the extension of the ulcerating process as they would similar traumatizing reactions, regardless of how they are transmitted. The pain position and reference of the pain depend on the particular structure involved, and the severity depends on the extent and violence of the offending pathologic process. This is a distinct syndrome produced by a separate mechanism. The symptoms produced by perforating ulcer thus are the result of an interaction of two syndromes. The visceral one includes the usually understood symptoms of peptic ulcer while the somatic one consists of a more constant and more definitely localizable distress which often is only slightly affected, if at all, by methods which usually relieve visceral pain. There is a diagnostic key in the site and extension of this secondary pain because it generally is felt along the peripheral distribution of the nerves occupying the same segments which were invaded in their peritoneal distribution by the inflammatory products of penetrating or perforating ulcers. Hence, if the tissues of the lesser omentum are invaded, the pain as a rule is felt in the epigastrium and extends to the right or left costal region and to the midthoracic portion of the back. Should the anterior abdominal wall be involved, pain is produced which closely approximates the site invaded. It may spread ipsilaterally and to the back. Should the inflammatory processes caused by spreading ulceration invade the pancreas, the resultant pain most often will be felt about the level of the umbilicus and will extend to either the right or left. It extends through to the back to the region of the upper lumbar vertebrae. This pain is excruciatingly severe and patients often attempt to relieve it by certain postural methods such as assuming the knee-chest position or leaning forward with their knees drawn up tightly. Invasion of the mesocolon or the root of the mesentery of the small bowel generally produces pain which extends downward, occasionally as low as the hypogastric or the inguinal region.

*Perforating Peptic Ulcer Syndrome with a Somatic Syndrome Replacing the Visceral Syndrome*:—In a case of penetrating ulcer the inflammatory metabolites occasionally cease to irritate the somatic structures as the ulcer begins to heal. The reference of pain into other regions then may stop completely and the visceral syndrome in its pure form may be re-established. Not infrequently, however, the pathologic condition progresses; the somatic structures become the seat of marked

inflammatory reaction and an abscess may develop. When this occurs, the somatic syndrome may overpower the visceral one and completely obliterate it. There will then develop signs of peritoneal irritation, including marked tenderness. Occasionally, rigidity will develop over the site of the inflammation. Frequently there will then be no remaining symptoms which exhibit the characteristics usually assumed to indicate the presence of a peptic ulcer.

*Phrenic Peptic Ulcer Syndrome*:—Occasionally a gastric ulcer or an anastomotic ulcer which develops after the performance of a high partial gastric resection with antecolic gastrojejunostomy perforates and invades the diaphragm. The characteristic symptoms which actively suggest a peptic ulcer will then become complicated by signs suggesting invasion of the phrenic nerves. There will then be an extension of pain into the cutaneous area supplied by nerves from the same cervical segments to which the phrenic fibres are distributed. It can be seen that the pain would be interpreted by the patient as existing in the base of the neck, the supraclavicular region and the tip of the shoulder on the side on which the phrenic nerve was irritated.

In planning the course of therapy for a peptic ulcer, consideration must always be given to the possibility that such a lesion may contain some malignant cells. This applies almost exclusively to gastric ulcers. The microscope is the only certain means of making such diagnosis.

## Treatment of Peptic Ulcer

I have considered some of the ways and means of obtaining accurate knowledge of the pathologic state of the ulcer in an individual case. I have devoted much time to consideration of the tools of ulcer formation and various forms, or types, or etiologic groups of this disease. I believe that even the most skeptical reader will agree that no single immutable formula for the formation of peptic ulcer is conceivable. How can one colligate the etiologic pattern of a gastric ulcer associated with a foreign body, the frequently recurring duodenal ulcer associated with serious neurogenic factors and elevated secretory rates, the hemorrhagic ulcer which develops after a child has had tonsillitis and the peptic ulcer which occurs in the ileum which erroneously has been anastomosed to the stomach. It is not so important whether these are considered different types of peptic ulcer or merely varying phases of the same disease. What is important is the necessity of appreciating that the behavior of these ulcers, the prognosis, the tendency to recurrence, the ease of reactivation and, particularly, the treatment demand special consideration in individual cases.

*Selection of Medical or Surgical Treatment*:—In my opinion this decision is one of the most important steps in ulcer therapy. Too often its choice depends somewhat on the fact that the patient is being treated by a surgeon or an internist. At other times it hinges upon the fact that either the patient or his physician has become discouraged by the failure of several haphazard efforts at therapy and they are too busy or too impatient to devote the time or the patience to the serious business of intensive therapeutic efforts.

Frequently the indications for or against surgical treatment are not clear-cut and definite, even when accurate knowledge is available regarding the pathologic condition of the ulcer or its cause. The problem can best be considered if ulcers in different sites are discussed separately.

*Recurrence of Peptic Ulcer After Operation*:—The success of any surgical procedure instituted for peptic ulcer depends mainly on three accomplishments: (1) the stomach must be made to empty normally, (2) the impingement of the chyme must not be intensified so that it will bombard a certain area relentlessly, (3) the concentration of hydrochloric acid must be lowered appreciably. Failure to accomplish these objectives, and especially the last, usually results in further ulceration. After an ulcer is permanently established, perforating characteristics or other complications usually develop rapidly. Therapy for such ulcers, whether they occur after pyloroplasty or after gastrojejunostomy, is usually surgical. Preliminary medical treatment may be justifiable in cases in which the symptoms are mild. Occasionally, this succeeds, especially if instituted early in the course of a recurrent ulcer.

*Gastric Ulcers*:—To be dogmatic in opinions regarding therapy in any case of peptic ulcer is to invite justifiable criticism. It is, therefore, necessary to qualify the opinion which is prevalent at the clinic; namely, that gastric ulcer should be treated surgically. Perhaps we should say that we usually believe that gastric ulcer should be treated surgically unless other factors exist which make a trial of medical treatment advisable. In some cases of gastric ulcer, patients insist on medical therapy. Unless certain suggestive signs of malignancy are present, we usually acquiesce to their desires. If the ulcer is more than 2 cm. in diameter, if it is situated on the greater curvature, if gastric analysis reveals achlorhydria or a minimal amount of hydrochloric acid, or if the results of roentgenologic or gastroscopic examination cause us to suspect that the ulcer is malignant, we usually refuse to treat the patient medically. Furthermore, if patients who have such ulcers or have ulcers that are less suggestive of malignancy fail to show clinical, roentgenologic or gastroscopic signs of improvement or continue to have blood in the stools, medical therapy is discontinued after a reasonable time, usually in two to three weeks, and operation is advised.

In some cases in which the ulcer is believed to be malignant, the risk of operation would be greater than the risk of assuming that the ulcer is benign and treating the patient medically. In cases of small ulcer on the lesser curvature in which the concentration of hydrochloric acid is normal or increased and gastroscopic findings suggest that the ulcer is benign, we sometimes advise a trial of medical treatment if the patient can be observed carefully at frequent intervals for several years.

*Duodenal Ulcer*:—Uncomplicated duodenal ulcer usually is considered to be a medical problem. By making an accurate diagnosis and by evaluating the etiologic factors in a particular case, it is possible to plan the treatment with a reasonable expectation of success. I have considered in detail the different syndromes caused by a peptic ulcer in its life cycle. This information should enable one to make an

accurate diagnosis. I have stressed the importance of the complications. This information should be used in deciding whether a duodenal ulcer should be treated medically or surgically. Dr. Morlock, one of my associates, has said that the indications for the surgical treatment of a duodenal ulcer are as follows: "(1) failure of the ulcer to heal under good medical treatment, even though the lesion is objectively uncomplicated; (2) acute, subacute and chronic perforation and a lesion of large size, particularly if it has perforated into a neighboring viscus; (3) impairment of gastric motor function owing to inflammatory pyloric obstruction, cicatricial pyloric change or extensive perigastric and periduodenal adhesions; (4) repeated massive hemorrhage; (5) associated disease of the gallbladder or appendix or a concomitant gastric ulcer, and (6) environmental and economic factors interfering with maintenance of an adequate medical regimen."

*Rationale of Ulcer Therapy*:—The life cycle of a peptic ulcer includes little that is fixed and static. It is obvious that through it move several forces which are constantly changing in potency; chemical or mechanical forces of aggression stand opposed by forces through which the tissues are protected; now local and now systemic disturbances add potency to one or the other of these factors and influence the balance which results in healing, persistence or progression of the ulcerating process. Obviously, the contending play of these forces must be understood and given special and individual consideration in the therapeusis of this disease. No prearranged ready-made treatment is therefore possible. Furthermore, since it is often impossible for patients who have peptic ulcer to live under the constant watchful supervision and guidance of their physician, it is obvious that these patients must understand something about the problems incident to their disease and become a trained partner in contending with these problems as they arise. For this reason we often hospitalize these patients for a brief period of education as well as for instituting a medical and dietetic regimen so that the varying factors which seem important in the cause of this disease can be detected and therapy advised accordingly. The patients are remarkably interested in this instruction and with this comes a new understanding of their problems. Consequently, a spirit of cooperation develops wherein lies much hope for a greater eventual success in the handling of this disease.

*Control of Symptoms and Treatment of Complications*:—The symptoms of peptic ulcer are mainly the result of hyperacidity, hyperspasticity of gastrointestinal musculature, gastric stasis, hemorrhage, invasion of somatic structures by inflammatory product of perforation and certain systemic manifestations incident to these complications. The first prerequisite is to recognize complications. This includes a careful study of cellular and extracellular chemical reactions. Proper methods of treatment must be expeditiously carried out or the life of the patient may soon be in serious danger. Unless some grave complicating factor supervenes, it is, as a rule, not difficult to control the symptoms of peptic ulcer. These are controlled with greater facility if the patient is kept in bed. Hyperacidity can usually be counteracted by frequent feeding of some bland substance such as milk, and by the judicious use of alkalis, colloidal aluminum hydroxide or magnesium trisilicate.

Hyperspasticity responds admirably, as a rule, to the use of drugs which relax smooth muscle such as belladonna or such substitutes such as syntropan (the phosphate of 3-diethylamino-2, 2-dimethylpropylester of tropic acid), novatrine (homatropine methylbromide) and trasentine (a synthetic ester of diphenyl acetic acid and diethylaminoethanol) together with sedatives such as a barbiturate or a bromide.

*Planning a Regimen To Promote Adequate Healing*:—Experimentally produced peptic ulcer in animals requires about six weeks to heal when normal continuity of tissues and physiologic environment have been re-established. Medical therapy for ulcer in the human being can scarcely be expected to completely reverse the physiologic mechanisms responsible for such a lesion; therefore, it is safe to assume that even though successful treatment is carried out it will take several months to heal an ulcer completely. One of the most common causes of therapeutic failure is due to the presumption that quiescence of symptoms indicates that the lesion has healed. Vigilance in treatment is then relaxed and the patient returns to the usual routine of life to await the next disturbance in physiology which rapidly precipitates a new episode of symptoms and activity of the ulcer. Had the ulcer been thoroughly healed it is reasonable to assume that a minor or temporary increase of the aggression mechanism or a diminution of the cellular defense factors might not have resulted in reactivation of the lesion.

After the acute symptoms of ulcer have subsided and complications have ceased to be an active threat to the patient's life, it becomes possible to evaluate all available data more leisurely and meticulously. This particular stage in the treatment of ulcer is a very important one. It is here that accuracy in diagnosis becomes of real value. Specialized etiologic factors can be investigated. Secretory rates should be studied. If an associated disease is present, it must be evaluated in relationship to the ulcer and its treatment.

The healing of ulcer requires not only the mitigation of the acid factor but also the restoration and the maintenance of normal resistance of tissues. Effort to accomplish the former requires first of all the selection of a correct diet. This should be nonirritating and must contain the various food elements in proper balance, including vitamins and minerals. In addition, the diet should not abnormally provoke the secretion of acid and it should be able to neutralize acid by combining with it. It seldom is necessary to restrict the intake of food drastically for long periods. The amount and variety of food taken is increased rapidly so that within eight to ten days the patients are usually taking a pleasant, adequate, bland type of diet. Some dietetic precautions are continued for six to twelve months, during which time supplementary feedings between meals and at bedtime are advised.

The adequate reduction of acidity usually requires the use of antacids. The use of antispasmodics and sedatives also is advisable. During the early months of treatment, antacids are prescribed at 10 a.m., 2 p.m., 4:30 p.m., 7:30 p.m. and at bedtime. The use of antispasmodics and sedatives must be adjusted to the nervous tension exhibited by the individual patient.

Any plan of treatment for peptic ulcer must include provision for the search and eradication of such causes as seem capable of injuring gastroduodenal tissues. The proper recognition of the type of ulcer becomes of obvious value. Special treatment must then be applied to counteract the particular etiologic factor predominantly important in the specific case. Innocuous disturbances such as common colds or mild infection of the upper respiratory tract often precipitate a recurrence of symptoms. Hygienic measures to avoid these disturbances so far as possible are part of the treatment. The eradication of foci of infection in special cases may aid appreciably in controlling the activity and preventing the occurrence of peptic ulcers. Apart from dealing with infections of the teeth, tonsils, accessory sinuses and the prostate gland, surgical treatment at times has to be directed to the gallbladder and appendix if clinical evidence suggests retained infection in these organs.

Care must be taken that the lack of necessary accessory food factors arising from prolonged and enthusiastic adherence to a restricted diet does not mitigate against rather than assist in the healing of ulcers. There are other instances in which special local attention to traumatizing influences will result in the prompt cure of such lesions. One need only consider as examples bezoar or diaphragmatic hernia associated with gastric ulcer. In such cases, prompt cure of the ulcer results when the cause of the irritation is removed or corrected.

*Prevention of Recurrence*:—Statistical evidence indicating the frequency of recurrence of peptic ulcer has painted a picture of therapeutic futility which indeed is grafted onto our conception of what constitutes the ulcer syndrome. Although it is true that the individual breakdown of tissue is a mere link in the chain of the life cycle of ulcer this chain can frequently be broken by adequate treatment and thorough cooperation of the patient. This can only exceptionally be accomplished by a diet book, some pills and a pat on the back. It usually requires thoughtful evaluation of symptoms, tact and patience on the part of the physician, and a corresponding effort by the patient to understand his own disease and to accept some of the responsibility for the treatment.

The first requisite in the prevention of the recurrence of a peptic ulcer is the proper selection of medical and surgical therapy. The selection of patients for surgical treatment has been considered previously. Medical treatment is most satisfactory in cases in which noncomplicated ulcer produces symptoms which have been classified as the visceral ulcer syndrome. Between these two extremes there is a group of cases in which surgical treatment is not possible because of economic factors, the poor condition of the patients or the refusal of the patients to undergo an operation. Medical treatment, therefore, must be used in these cases. This type of treatment also may be used in a few cases of chronic perforating ulcer but the results usually are disappointing.

The requisites for the surgical prevention of recurrence of a peptic ulcer are clear-cut. The successful prevention of the ulcer is directly dependent on the extent

to which these requisites can be accomplished. There are a few physiologic facts which influence the recurrence of a peptic ulcer.

A peptic ulcer is produced by a mixture of hydrochloric acid and pepsin in the gastric chyme. If the concentration of these substances is abnormally high, or if the resistance of the mucosa is decreased, erosion may occur and an ulcer may develop.

The site of the ulcer usually is determined by a mechanical factor depending upon which regions are traumatized most vigorously or which regions have lost their resistance to the greatest degree. There are four distinct factors, namely, infectious, nutritional, traumatic and chemical, which can exert their influence upon the formation of an ulcer. They vary in different cases and so does the constitutional diathesis which must produce ulceration by the same means. Either the erosive factor is increased or the defense breaks down. The impulses which are responsible for hyperacidity in all probability are also responsible for hyperspasticity. The intermediary mechanisms responsible for these may originate in the vagus nerve and the endocrine glands or the hormones, but there seems little doubt that usually they originate in the cortex. At times the etiologic factor may originate in the intermediary mechanisms. The accumulation of these impulses is somehow accomplished by disturbances in the higher nerve centers. They overflow into the vagal funnel and the diathesis factor points the funnel not so much into the vascular or endocrine system but mainly into gastrointestinal channels. As a result, ulcer rather than hypertension, vascular disease or endocrine disturbances develop.

*Control of the Acidity of the Gastric Contents*:—Certain dietetic precautions are therefore a permanent part of the treatment of peptic ulcer. Highly spiced or poorly digestible foods should be avoided. Some bland food or milk concentrate tablets and an antacid should be taken midway between meals and at bedtime. This practice should be continued for an indefinite period. Drinks containing caffeine should not be taken. Alcohol and tobacco should be avoided by the patient with known persistent elevation of secretory rates, and should be used only in moderation shortly before or after meals by any patient with peptic ulcer. During periods of stress, fatigue or infection, or after dietetic prudence has been impossible for a few days, antacids and supplementary feedings should be taken several times between meals for three or four days. It is hoped that some substance such as enterogastrone or urogastrone will turn out to be of some help in insuring a permanent retardation of secretory rates. This would be a great aid in preventing recurrence of ulcer.

*Maintenance of Normal Resistance of Tissues*:—Precautionary measures to avoid colds or respiratory infection are important in accomplishing this requirement. Food faddism should be avoided. Food must contain adequate amounts of calories in proper balance, and vitamins and minerals. The slight anemia which often is noted in cases of peptic ulcer should be counteracted by the daily or periodic use of iron, preferably in the form of enteric-coated pills. Foci of infection should be eradicated. In short, any measure which tends to improve or maintain

the patient's general health will increase his resistance to chemical processes which will cause the reactivation of a peptic ulcer.

*Treatment of Constitutional Diathesis*:—The interrelated mechanisms which make up a constitutional diathesis are imperfectly understood. The psychophysiologic type of diathesis appears to be most important in the production of peptic ulcer. Whether this type of diathesis is primarily psychologic or physiologic is not important because these factors are closely related. The prevention of recurrence of peptic ulcer is largely dependent on the recognition and control of constitutional diathesis. This represents one of the most important and fascinating phases of the treatment of peptic ulcer. To accomplish this it is necessary that the patient be made a responsible partner in treatment. He must understand something about the manner in which his habits can affect his gastric function. Frequently when lectures are given to patients under hospital care, they exhibit great interest in anatomic and physiologic discussions and they soon learn to apply the acquired information to their personal problems. They begin to understand that success in treatment depends in a large degree upon themselves. With the dawn of this understanding comes a cooperation which is heartening to their physicians and which bodes well for the success of the treatment. It is absolutely essential that the patient should understand that his disease remains a perennial problem. He should be made to understand that at certain times the tendency for the ulcer to recur is increased and that at these times additional precautions are necessary.

The patient and resident physician who understand the problems of ulcer therapy meet frequently for group discussion. The importance of the nervous system in relationship to the cause and recurrence of ulcer is discussed. It is pointed out how nervous tension, worry, fatigue, and abnormally responsive mental reactions to the trials and difficulties of life are likely to affect the development and the life cycle of peptic ulcers.

At individual conferences with his physician, each patient is given the opportunity of discussing his own personal problems and their relationship to his disease. Patients at first frequently deny the relationship of periods of worry and strife to their symptoms but close questioning and observation leave little doubt as to the relationship between the two. Some patients' composure and external appearance of calmness and tranquillity leave a veritable turmoil of emotions which remains submerged and unsuspected until careful study and kindly, sympathetic investigation stimulates the understanding and confidence which brings it to light. When the importance of these nervous factors is discussed with the patient, he frequently begins a search through his past experiences and often, to his own surprise, he is able to satisfy himself of the interrelation of his troubles and his symptoms. With this understanding come confidence and then cooperation. The battle then is half won. It becomes easy to convince the patient that it is necessary for him to avoid unusual fatigue or unnecessary responsibility even when he is feeling well. It often is possible to change the patient's mental reaction to the usual disquieting influences incident to daily life. A serious obstacle which blocks the way

to recovery can be removed if the patient can be taught to accept these experiences less impetuously, to do things with less speed and intenseness, and to develop a spirit of equanimity toward incidents which tend to perturb him.

Sometimes it is necessary for these patients to give up some of their avoidable responsibilities in club, church, philanthropic or social activities. It may actually become obligatory to make some change in their business or professional relationships. At times it is possible for the patient to arrange his work to devote some time each day for play or for the pursuit of some hobby. Frequently, properly planned vacations are beneficial. A short rest after the noon meal is advisable. I have been able to convince some club officials to install a quiet, dark room in their club so that members so inclined can retire for a short repose after lunch in an environment free from noise and agitation. The patient should also utilize the occasion of the supplementary feeding he takes between meals to obtain a brief respite from work and worry. Nine or ten hours of sleep at night is advisable, and if this is not possible without sedatives I frequently advise the use of small amounts of bromides or barbiturates.

The requirements which I have outlined for the prevention of recurrence in peptic ulcer are difficult to accomplish. They make great demands on the time and on the patience of the physician. They also require a vigorous effort on the part of the patient, which, however, is not an unsurmountable task if the determination to remain well is sufficiently sincere and if an intelligent partnership in treatment has been accomplished.

# TREATMENT OF GASTRODUODENAL PEPTIC ULCERS WITH PROTEIN HYDROLYSATE AND A NONREACTIVE ALUMINUM HYDROXIDE PREPARATION*

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The direct cause for peptic ulcer is an egence, the nature of which is still unknown. In consequence, the literature abounds with recommended treatments. The parts played by readily absorbable and digestible well balanced diets and antacids in the production of relief from peptic ulcer symptoms is too well known to merit repetition.

The purpose of this paper is three fold: 1) To present the basis for a recommended routine of treatment of peptic ulcer patients, the treatment consisting of protein hydrolysate and a nonreactive aluminum hydroxide gel mixture; 2) To report the effects on the patients studied and 3) To evaluate these effects in comparison to two other studies.

## Basis and Treatment

Chronic peptic ulcers are practically always complicated by varying degrees of chronic gastritis. Digestion and subsequently absorption of food is thereby hampered. Elman[1] has stressed the effect of protein deficiency in restricted diets. While the protein content of an ulcer diet can be supplemented with milk, protein hydrolysate is more readily broken down from its polypeptoids to available amino acids which in turn are easily absorbed. Levy[2] reported that a solution of 10 per cent amigen in 10 per cent glucose when given orally via a constant drip through a Levine tube or in amounts of 90 cc. every hour was well tolerated by bleeding peptic ulcer patients. Further, "the serum protein returned to normal, on the average, within 10.2 days". In a previous report[3] on the treatment with protein hydrolysate of ambulatory peptic ulcer patients for a period of one year I also found that the medicament was well tolerated.

Levy and Siler[4] had demonstrated that an amino acids mixture had antacid qualities in the human stomach. In an auxiliary study[5] to the one previously mentioned, I demonstrated last year that the antacid effect of protein hydrolysate in doses up to 50 grams lasted only for 1 to 1½ hours. At the end of that time the protein hydrolysate had a gastric secretagogue effect. In a personal communication Bockus[6] recently informed me that his associates, Berk and Lopusniak, confirmed this finding.

In order to avail the peptic ulcer patient of the nutritional benefits of protein hydrolysate and at the same time to control its secretagogue effect I suggested[5] that *another* antacid be used one hour *after* protein hydrolysate. Since the amount of supplementary amino acids needed is generally slight, another antacid rather than

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another dose of protein hydrolysate was decided upon. A supplement of 50 grams of protein hydrolysate per day divided into three doses was arbitrarily chosen. The remaining 100 grams of the daily requirement of protein being supplied via diet, made up the average total daily requirement of 150 grams of protein per patient.

Hoffman and Deniwitz[7] in their report on the effect of *alumina gel* upon the *absorption* of amino acids from the intestinal tract concluded that in therapeutic doses alumina gel had *no* demonstrable effect. The antacid chosen for the investigation that I am now reporting was a nonreactive aluminum hydroxide gel preparation. When nonreactive alumina gel preparations are used there is either

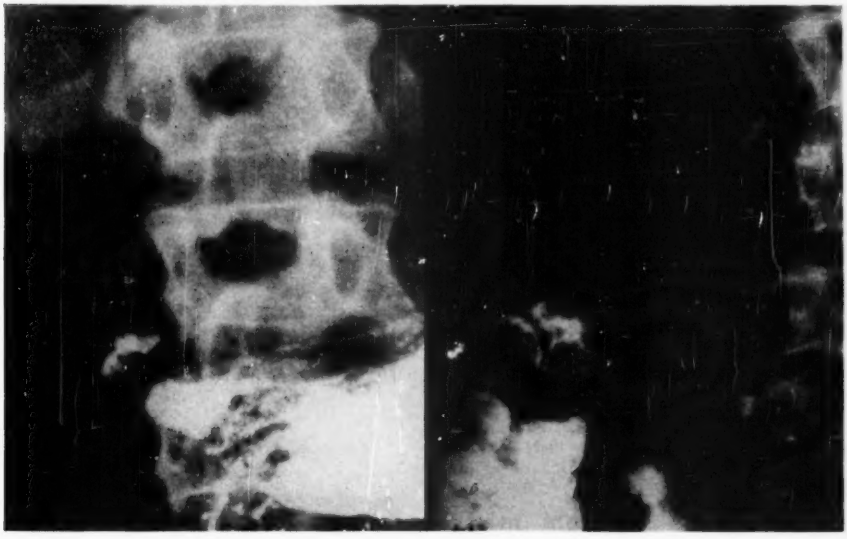

Fig. 1a Fig. 1b

Fig. 1—Case 3. a) Active duodenal ulcer before treatment. b) 6 hour barium in crater, before treatment.

a "decreased incidence of—constipation in patients"[8] or the effect is "not constipating at all"[9]. Two fluid drams of the antacid mixture was the dose used in this study.

Peptic ulcer patients derive greatest relief from treatment if the medications are given in *anticipation* of the occurrence of symptoms rather than when the symptoms *present themselves*. The periodicity with which the symptoms *appear* simplifies the anticipation of their arrival. The routine for administration of the aforementioned medicaments is as follows:

8 A.M. Breakfast
9 A.M. Antacid mixture
10 A.M. Protein hydrolysate
11 A.M. Antacid mixture

12 Noon Luncheon
1 P.M. Antacid mixture
2 P.M. Protein hydrolysate
3 P.M. Antacid mixture
6 P.M. Dinner
7 P.M. Antacid mixture
8 P.M. Protein hydrolysate
9 P.M. Antacid mixture
10 P.M. Retire for the night

If symptoms develop between 4 and 6 P.M. or after 10 P.M., an extra dose of the antacid mixture was used.

## Clinical Material

This series comprises fifteen patients. At the onset of this study all but one (case 11) presented clinical and roentgenological evidence of active peptic ulceration. The latter was clinically and roentgenologically a case of peptic ulcer symptom complex. At the end of his twenty-first week of treatment an inactive lesser curvature duodenal cap ulcer was observed on x-ray study.

It was impractical to start and complete all of the patients on treatment at the same time. Consequently, cases 2, 3 and 12 were under treatment through eighteen weeks and case 8 was studied through thirteen weeks. Patient 4 was discontinued at the end of the sixth week due to change of locale, as was also 12 at the end of the eighteenth week.

This group consisted of five females ranging from 35 to 70 years of age and ten males from 29 to 55 years of age. The youngest patient was a male. There were four males and one female in the 30 through 39 year age group; two males and two females in the 40 through 49 year age group; three males and one female in the 50 through 59 year age group. The oldest patient was a female.

The length of time from which the patients had been diagnosed as peptic ulcer cases varied from three weeks to twenty-five years before this treatment. Four patients had their first episode of ulcer symptoms and x-ray evidence just prior to onset of this study. One was diagnosed only three weeks before this treatment was started. Three patients were aware of the diagnosis for two years; on four the diagnoses were made four to five years preceding this investigation. Each of the remaining three cases were diagnosed as peptic ulcer patients 16, 24½ and 25 years ago.

Two of the male patients had gastric ulcers, one had his ulcer at the juncture between the first and second portions of the duodenum, and seven ulcers involved the duodenal cap. The five females had their ulcers in the duodenal cap.

Both of the gastric ulcers were on the lesser curvature in the prepyloric region. Six of the duodenal cap ulcers were on the lesser curvature. Each one of three patients had their duodenal cap ulcer on the posterior wall, apex or lesser and greater curvatures. As mentioned above, one patient had his ulcer at the juncture between the first and second portion of the duodenum. Deformities of three of the duodenal caps precluded definite location of the ulcer niche.

Patients were considered as experiencing hunger-pain if they complained of a pain having most of the following characteristics: epigastric gnawing sensation; relieved by food or alkali; recurred periodically about one to two hours after meals; tended to recur during the night and in the spring and fall of the year. Where there was no other corroboratory evidence, hunger-pain, that did not conform to the pattern just described, was not interpreted as the result of an existing ulcer. Hunger discomfort may be due to the ingestion of insufficient food bulk, to gastric hyperacidity, excessive smoking, early gastric neoplasm, duodenitis, gastric or small intestinal diverticula, chronic cholecystitis, chronic appendicitis[10], and spontaneous[11] or insulin[12] hypoglycemia. Although gastric contraction is thought to be essential for the development of the sensation of hunger, it had been noted as occurring after a total gastrectomy[13].

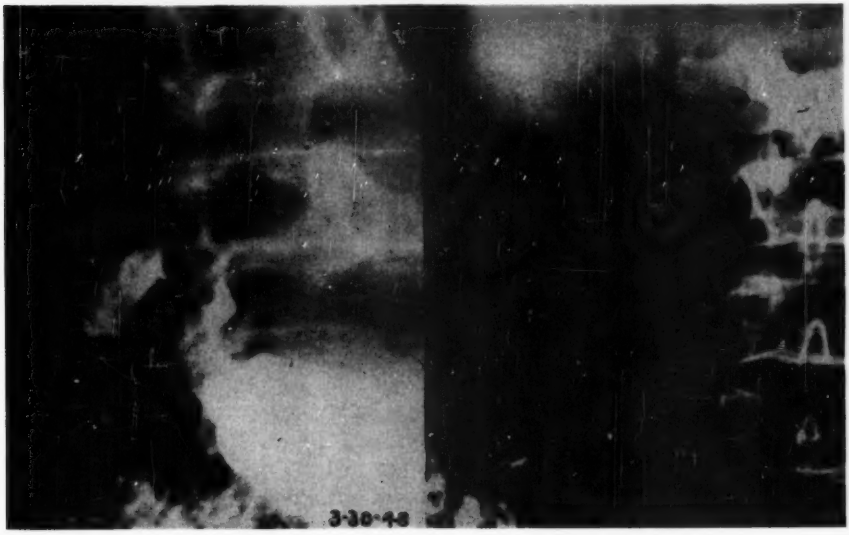

Fig. 2a Fig. 2b

Fig. 2—Case 3. a) Inactive after treatment. b) 6 hour, no barium in crater, after treatment.

The laity varies widely in the interpretation of constipation. Some patients believe that they are constipated if they expel formed feces and the first fecal segment is hard, or have less than two bowel movements daily or if they do not defecate every day. The patients under study were considered constipated if they complained of a sensation of incomplete bowel evacuation and/or an increase in their average interval between defecation.

## Procedure

A detailed history and physical examination was carried out on each patient. The gastrointestinal tract was studied via roentgenoscopy and roentgenography before treatment was instituted except in case 6. That patient was seen for the

TABLE I

SYMPTOMS BEFORE TREATMENT

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sex | F | M | M | F | M | F | M | M | F | M | M | M | F | M | M | |
| Age | 48 | 30 | 37 | 41 | 46 | 35 | 29 | 41 | 58 | 50 | 55 | 52 | 70 | 30 | 34 | |
| Wt. at onset | 207¾ | 119½ | 159¾ | 125¾ | 158 | 135 | 129½ | 192 | 148½ | 171 | 145 | 150 | 160½ | 166 | 176½ | |
| Appetite | good | poor | poor | fair | good | good | fair | good | good | fair | fair | good | good | good | good | |
| Hunger-pain | 0 | 4+ | 2+ | 0 | 4+ | 3+ | 2+ | 0 | 1+ | 1+ | 4+ | 3+ | 3+ | 1+ | 2+ | |
| Belching | 2+ | 0 | 0 | 4+ | 0 | 0 | 0 | 2+ | 0 | 1+ | 3+ | 0 | 1+ | 3+ | 0 | |
| Heart-burn | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3+ | 1+ | 0 | 0 | 0 | |
| Nausea | 0 | 0 | 1+ | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | |
| Vomiting | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 1+ | 0 | 0 | |
| Abd. pain | 2+ | 4+ | 4+ | 4+ | 4+ | 3+ | 0 | 2+ | 0 | 0 | 1+ | 2+ | 0 | 3+ | 0 | |
| Diarrhea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Constipation | 3+ | 0 | 4+ | 0 | 0 | 0 | 0 | 0 | 2+ | 1+ | 2+ | 3+ | 0 | 0 | 0 | |
| 1st learned of ulcer | 25 yrs. ago | 4 yrs. ago | Now | 24½ yrs. ago | Now | 5 yrs. ago | Now | Now | 5 yrs. ago | 2 yrs. ago | 3 wks. ago | 2 yrs. ago | 16 yrs. ago | 5 yrs. ago | 2 yrs. ago | |
| X-ray findings and remarks | Active duo. cap ulcer on posterior wall. | Active ulcer at juncture of 1st and 2nd portions of duo. | Active duo. cap ulcer. | Active duo. cap ulcer on apex. | Active duo. cap ulcer with deformity. | Active bleeding therefore x-ray delayed. | Active duo. cap ulcer. | Active duo. cap ulcers on both curvatures. | Active duo. cap ulcer. | Active gastric antral ulcer with marked hypertrophic gastritis. | Symptom complex of active duo. cap ulcer. | Active duo. cap ulcer. | Active duo. cap ulcer with clover-leaf deformity. | Active duo. cap ulcer with chr. gastritis and chr. duodenitis. | No ulcer seen. Gastroscopically a small prepyloric ulcer. | |

TABLE II

SYMPTOMS TWO THROUGH FIVE WEEKS WITH TREATMENT*

| Case | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | 7 | | 8 | | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Weeks | 2 | 4 | 2 | 4 | 2 | 4 | 2 | 4 | 2 | 4 | 3 | 2 | 4 | 2 | 5 | 4 | 5 | 5 |
| Weight | 211 | 212 | 120¼ | 120½ | 168 | 168½ | 128½ | 129 | 166 | 167 | 133½ | 130¼ | 132¾ | 189¾ | 188¼ | 149 | 175 | 147 |
| Appetite | good | good | good | good | good | good | good | good | good | good | good | good | good | good | good | good | good | good |
| Hunger-pain | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | 1+ | 1+ | 3+ | 0 | 2+ | 0 | 0 | 3+ | 0 | 2+ | 0 |
| Belching | 0 | 0 | 0 | 0 | 0 | 1+ | 1+ | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 |
| Heart-burn | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | 2+ | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 |
| Nausea | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Vomiting | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 time | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Abd. pain | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 3+ | 0 | 2+ | 1+ | 1+ | 0 | 0 | 0 | 0 |
| Diarrhea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Constipation | 0 | 1+ | 0 | 0 | 4+ | 0 | 2+ | 2+ | 1+ | 3+ | 0 | 4+ | 0 | 1+ | 1+ | 0 | 1+ | 0 |
| X-ray findings and remarks | | | | | | | | | | | Recovered from bleeding. Slight duo. cap ulcer with deformity. | | | | | | | Slight active duo. cap ulcer. |

*NOTE: Patients 12-13-14 and 15, did not report in for study, but continued treatment.

first time during a bleeding episode. In that instance x-ray study was carried out three weeks after the onset of this treatment.

All of the patients were given the same bland, low residue and high caloric diet. A multivitamin emulsion mixture was ordered. Protein hydrolysate in one-half ounce doses, dissolved in one-half a glass of milk, fruit juice or soup was to be taken two hours after each of the three main meals. Two fluid drams of a nonreactive aluminum hydroxide gel mixture containing ¼ grain of sodium phenobarbital and 1/200 grain of atropine sulphate was to be taken with water one hour and again three hours after meals.

As recorded on the accompanying tables all of the patients continued the above treatment throughout their period of study. This was determined not only

Fig. 3a Fig. 3b

Fig. 3—Case 5. a) Active duodenal ulcer before treatment. b) 6 hour barium in crater, before treatment.

by the patients' statements but also by the calculated time that the medications given to them should last before they returned for another supply.

The irregularity of the time element that the patients reported in for study was due to the fact that the patients were not all placed under study at the same time and also unforeseen circumstances prevented some of these patients from reporting for x-ray reexamination on the prescribed day or week.

The first roentgenological recheck was conducted on case 11 at the end of the fifth week of treatment. Ten cases were again x-rayed during the 6 through 9 week period; ten cases during the 21 through 40 week period.

The intensities of the symptoms were recorded when the patients reported for physical examination and/or x-ray study. The intensity was entered as zero, one plus, two plus, etc. depending upon its severity. It is appreciated that, not unlike all clinical studies depending upon the cooperation of the patient's ability to evaluate symptoms, there is a strong likelihood towards an element of error in their interpretation.

## Observations

*Appetite*:—Cases 2 and 3 had poor appetites before treatment was started. The appetite was fair in four of the patients. Nine had good appetites before treatment. The over-all picture in this series of patients is one where the peptic ulcer had little bad effect on the appetite. After the treatment was instituted all of the patients experienced an increase in appetite as was manifested by a request that

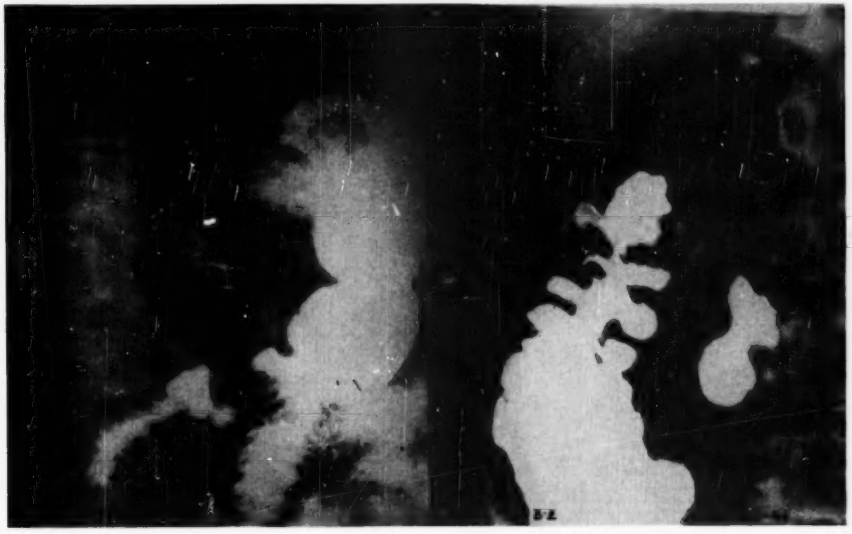

Fig. 4a Fig. 4b

Fig. 4—Case 5. a) Inactive after treatment. b) 6 hour barium still in crater after treatment.

their prescribed food intake be increased in amount. This is contrary to the findings reported with the use of protein hydrolysate by some other observers. In the previously mentioned study[3] of protein hydrolysate treatment on eighteen peptic ulcer patients over a period of almost one full year it was also noted that the appetite was not thereby impaired. This may be due to the product used or to the psychological approach to the patient.

For best cooperation on the part of the patient it seems logically advisable to forewarn him of the odor and taste of that medicament and to immediately impress him of favorable symptomatological effects that it could have in his case. In several instances I have heard physicians describe protein hydrolysate to their patients

TABLE III

SYMPTOMS SIX THROUGH NINE WEEKS WITH TREATMENT*

| Case | 1 | 2 | 3 | 4 | 5 | | 6 | 7 | 8 | 9 | 10 | 12 | 13 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Weeks | 6 | 6 | 6 | 6 | 7 | 8 | 7 | 8 | 7 | 9 | 8 | 6 | 7 | |
| Weight | 210 | 123¼ | 170 | 127 | — | 164½ | 133½ | 128½ | 184¾ | 148½ | 174 | 147½ | 158 | |
| Appetite | good | good | good | good | good | good | good | fair | good | good | good | good | good | |
| Hunger-pain | 0 | 0 | 0 | 0 | 1+ | 1+ | 0 | 1+ | 2+ | 0 | 0 | 0 | 1+ | |
| Belching | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 1+ | |
| Heart-burn | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 0 | |
| Nausea | 0 | 1+ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | |
| Vomiting | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Abd. pain | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | |
| Diarrhea | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | 0 | 0 | 1+ | |
| Constipation | 0 | 0 | 0 | 2+ | 2+ | 1+ | 0 | 0 | 0 | 1+ | 0 | 0 | 0 | |
| X-ray findings and remarks | Inactive duo. cap ulcer on posterior wall. Niche smaller. | | Inactive duo. ulcer at juncture between 1st and 2nd portions. | | Inactive duo. cap ulcer. Niche smaller. | | Less active duo. cap ulcer. | | Slightly active duo. cap ulcer. | | Inactive duo. cap ulcer with deformity. | | Still active duo. cap. | Less active duo. cap ulcer. | Less active duo. cap ulcer. | Less active duo. cap ulcer. Deformity unchanged. |

TABLE IV

SYMPTOMS TEN THROUGH TWENTY WEEKS WITH TREATMENT*

| Case | 1 | 2 | 3 | 5 | 6 | 8 | 10 | 11 | 12 | 14 | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Weeks | 13 | 18 | 18 | 10 | 19 | 13 | 13 | 10 | 18 | 12 | 17 |
| Weight | 212½ | 122 | 174 | 161½ | 134¼ | 188 | 177 | 150½ | 157½ | 175 | 178 |
| Appetite | good | good | good | good | good | good | good | good | good | good | good |
| Hunger-pain | 0 | 1+ | 0 | 1+ | 0 | 1+ | 1+ | 0 | 0 | 0 | 0 |
| Belching | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2+ | 0 |
| Heart-burn | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Nausea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Vomiting | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Abd. pain | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Diarrhea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Constipation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | 1+ | 1+ | 0 |
| X-ray findings and remarks | Inactive duo. cap ulcer on posterior wall. Niche still smaller. | No ulcer seen. | Inactive duo. cap ulcer. Niche still smaller. | | Inactive duo. cap ulcer. Deformity unchanged. | Inactive duo. cap ulcer. | No ulcer seen. Pyloro-duodenal region slightly irritable. | | No ulcer seen. | No ulcer seen. | |

*NOTE: Patient 4 did not report in for study. Moved out of city. Patients 7, 9, 13 and 15 did not report in for study, but continued treatment.

for whom they had ordered this medicament, describing it in a most distasteful manner. They invariably defeated their purpose before treatment was even started. It is, however, conceded that some patients just cannot tolerate protein hydrolysate.

*Hunger-pain*:—Before treatment 13 of the 15 patients experienced hunger-pain of 1 to 4 plus intensity. At the 2 through 5 week period, only 6 of the 11 patients that reported for study had hunger-pain of 1 to 3 plus intensity. At the 6 through 40 week period only 4 of the 10 to 12 patients that reported for study had hunger-pain and that only of 1 plus intensity.

*Belching*:—Prior to treatment, 7 of the group compained of belching with the intensity varying from 1 to 4 plus. Three of the 11 patients that reported for

Fig. 5a Fig. 5b

Fig. 5—Case 7. a) Active duodenal ulcer before treatment. b) No ulcer after treatment.

study during the 2 through 5 week period belched with a 1 plus intensity. Of the 10 to 12 patients studied at the 6 through 40 week period only 1 to 2 patients were belching with a 1 to 2 plus intensity.

*Heart-burn*:—At the beginning of this study 2 patients stated that they had heart-burn of 1 to 3 plus intensity. During the 2 through 5 week period 3 of the 11 cases studied had heart-burn of a 1 to 2 plus intensity. For the remainder of the study none of the patients experienced heart-burn.

*Nausea*:—Three patients complained of nausea of 1 plus intensity prior to treatment. At the 2 through 9 week period of the 11 to 12 patients that reported for study, 1 to 2 had that symptom with a 1 plus intensity. None of the patients were nauseous throughout the remainder of the study.

*Vomiting*:—Three patients vomited slightly (1 plus intensity) before the study was started. Thereafter none of the patients vomited.

*Abdominal pain*:—Prior to treatment, 10 patients had abdominal pain of 1 to 4 plus intensity. Of these 8 had epigastric pain. One patient had right lower quadrant and one midabdominal pain. Pain of 1 plus intensity was present in 2 of the 12 patients that reported for study during the 6 through 9 week period. None of the 10 cases that reported for examination at the 10 through 20 week period complained of pain. Only 1 patient had slight pain (1 plus intensity) out of 10 that reported for study during the 21 through 40 week period.

*Diarrhea*:—Diarrhea was present only in 1 case and that of only 1 plus intensity before onset of treatment. One to 2 patients of the 11 to 12 cases studied during the 2 through 9 week period had diarrhea of 1 plus intensity. None of the cases experienced diarrhea thereafter.

Fig. 6a Fig. 6b Fig. 6c

Fig. 6—Case 11. a) Ulcer symptom complex before treatment. b) Active duodenal ulcer after treatment. c) Inactive duodenal ulcer after treatment.

*Constipation*:—Before treatment, 6 patients were constipated to the degree of 1 to 4 plus. During the 2 through 5 week period 7 of the 11 cases studied had constipation of 1 to 4 plus intensity. At the 6 through 20 week period 3 of the 10 to 12 cases that were reexamined were constipated with a 1 to 2 plus intensity. Only 2 of the 10 patients seen at the 21 through 40 week period were constipated with an intensity of 1 to 4 plus.

It is noteworthy that the incidence of constipation was reduced by 50 per cent. In the studies previously referred to it was demonstrated that protein hydrolysate[3] and also a nonreactive aluminum hydroxide gel mixture[9] had excellent effects in the relief from constipation.

*Weight changes*:—The entire study revealed an average weight loss of 4¼ pounds in two cases. One patient's weight remained stationary. Twelve patients gained an average weight of 5.72 pounds.

*X-ray data*:—a) Five patients presented no x-ray evidence of peptic ulcer at the end of their study. Of these cases, 2 had their lesions for 2 years and were

TABLE V

SYMPTOMS TWENTY-ONE THROUGH FORTY WEEKS WITH TREATMENT*

| Case | 1 | 5 | 6 | 7 | 9 | 10 | 11 | | 13 | 14 | | 15 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Weeks | 30 | 26 | 32 | 21 | 21 | 26 | 21 | 29 | 24 | 28 | 40 | 26 | 38 |
| Weight | 212½ | 165½ | 137 | 130½ | 151½ | 171¼ | 148 | 154½ | 160½ | 182 | — | 169 | 172 |
| Appetite | good | good | good | fair | good | good | good | good | good | good | — | good | good |
| Hunger-pain | 0 | 0 | 0 | 1+ | 0 | 1+ | 1+ | 0 | 0 | 1+ | — | 1+ | 1+ |
| Belching | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | 1+ | 2+ |
| Heart-burn | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | 0 | 0 |
| Nausea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | 0 | 0 |
| Vomiting | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | 0 | 0 |
| Abd. pain | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1+ | — | 0 | 0 |
| Diarrhea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | 0 | 0 |
| Constipation | 0 | 0 | 0 | 1+ | 4+ | 0 | 0 | 0 | 0 | 0 | — | 0 | 0 |
| X-ray findings and remarks | No ulcer seen. | Inactive duo. cap ulcer. | Inactive duo. cap ulcer. Deformity unchanged. | No ulcer seen. Duodenitis present. | Inactive duo. cap ulcer. | Slightly active duo. cap ulcer | Inactive duo. cap ulcer. | | Inactive duo. ulcer. Deformity unchanged. | Slightly active duo. cap ulcer. | Cholecystectomized. Healed ulcer seen. | Slightly active prepyloric ulcer. | No ulcer seen. |

*NOTE: Patients 2 and 3 did not report in for study, but continued treatment. Patients 4 and 12 study discontinued, patients moved out of city. Patient 8 still under treatment.

TABLE VI

SUMMARY OF DATA

| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Sex | F | M | M | F | M | F | M | M | F | M | M | M | F | M | M |
| Age | 48 | 30 | 37 | 41 | 46 | 35 | 29 | 41 | 58 | 50 | 55 | 52 | 70 | 30 | 34 |
| Ulcer diagnosed | 25 yrs. ago | 4 yrs. ago | Nov. 18-47 | 24½ yrs. ago | Sept. 22-47 | 5 yrs. ago | Nov. 10-47 | Feb. 7-48 | 5 yrs. ago | 2 yrs. ago | 3 wks. ago | 2 yrs. ago | 16 yrs. ago | 5 yrs. ago | 2yrs. ago |
| Treatment started | May 20 1947 | Dec. 6 1947 | Nov. 18-47 | Feb. 10 1947 | Sept. 22-47 | May 20 1947 | Nov. 10-47 | Feb. 7-48 | Oct. 9-47 | Oct. 16 1947 | July 14-47 | Aug. 22 1947 | Sept. 10-47 | Feb. 19-47 | Mar. 4 1947 |
| Weight at onset of treatment | 207¾ | 119½ | 159¾ | 125¾ | 158 | 135 | 129½ | 192 | 148½ | 171 | 145 | 150 | 160½ | 166 | 176½ |
| Last Weight | 212½ | 122 | 174 | 127 | 165½ | 137 | 130½ | 188 | 151½ | 171¼ | 154½ | 157½ | 160½ | 182 | 172 |
| Weight change | +4¾ | -2½ | +14¼ | +1¼ | +7½ | +2 | +1 | -4 | +3 | +¼ | +9½ | +7½ | 0 | +16 | -4½ |
| Initial x-ray findings | Active duo. cap ulcer on posterior wall. | Active ulcer at juncture of 1st & 2nd portions of duo. | Active duo. cap ulcer. | Active duo.cap ulcer. on apex. | Active duo. cap ulcer with deformity. | Slightly active duo. cap ulcer. | Active duo. cap ulcer. | Active duo. cap ulcers on both curvatures. | Active duo. cap ulcer. | Active gastric antral ulcer with marked hypertrophic gastritis. | Symptom complex of active duo. cap ulcer. | Active duo.cap ulcer. | Active duo. cap ulcer with clover-leaf deformity. | Active duo. cap ulcer with chr. gastritis & chr. duodenitis. | No ulcer seen. Gastroscopically a small prepyloric ulcer. |
| Final x-ray findings | No ulcer seen. | No ulcer seen. | Inactive duo. cap ulcer. Niche very small. | Less active duo. cap ulcer. | Inactive duo. cap ulcer. | Inactive duo. cap ulcer. Deformity unchanged. | No ulcer seen. Duodenitis present. | Inactive duo. cap ulcer. | Inactive duo. cap ulcer. | Slightly active duo. cap ulcer. | Inactive duo. cap ulcer. | No ulcer seen. | Inactive duo. ulcer Deformity unchanged. | Cholecystectomized & headed duo. cap ulcer observed. | No ulcer seen. Refused regastroscopic examination. |

under this treatment for 18 weeks; one case was diagnosed just before onset of this study and had been under this treatment for 21 weeks; one patient had her ulcer for 25 years and had had 30 weeks of the treatment under discussion.

The fifth case (case 15) did not present any ulcer before treatment. He was, therefore, gastroscoped and a small lesser curvature prepyloric ulcer was brought into view. At the end of 26 weeks of treatment this lesion was roentgenologically noted as being slightly active. At the 38th week, reexamination did not reveal the ulcer but the patient had some hunger-pain. He refused a second gastroscopic study.

b) Seven patients presented x-ray evidence of inactive chronic ulceration. If the lesion was noted but there was no irritability nor tenderness over that area and the patient was asymptomatic, the ulcer was considered as being inactive.

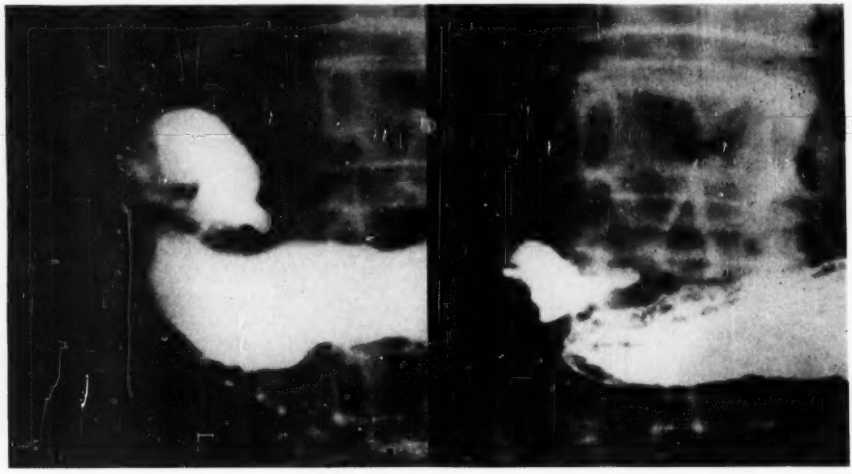

Fig. 7a Fig. 7b

Fig. 7—Case 13. a) Active duodenal ulcer before treatment. b) Inactive after treatment.

Two of these cases had ulcers of 5 years duration. One of these became inactive at the 7th week and remained that way for the balance of the 32 weeks of treatment. The other was inactive at the 21st week. The 70 year old woman had had her ulcer for 16 years and the lesion became inactive after 24 weeks of treatment.

Case 11 had been diagnosed as a peptic ulcer symptom complex patient 3 weeks prior to this treatment. He presented an inactive ulcer at the 21st week. The ulcers in the remaining three patients were observed just prior to this investigation. The lesion became inactive in case 3 at the 6th week and remained that way through the 18th week. The last two cases became inactive at the 13th and 26th weeks.

TABLE VII

SUMMARY OF SYMPTOMS

| | Before treatment | | 2 - 5 weeks treatment | | 6 - 9 weeks treatment | | 10 - 20 weeks treatment | | 21 - 40 weeks treatment | |
|---|---|---|---|---|---|---|---|---|---|---|
| Number of cases reported in for study | 15 cases | | 11 cases | | 12 cases | | 10 cases | | 10 cases | |
| Weight | 119½ - 207¾ lbs | | 120½ 212 lbs. | | 123¼ - 210 lbs. | | 122 - 212½ lbs. | | 130½ - 212½ lbs. | |
| Mean weight | 163.62 lbs. | | 166.25 lbs. | | 166.64 lbs. | | 167.25 lbs | | 171.5 lbs | |
| SYMPTOMS | No. cases | Intensity | No. cases | Intensity | No. cases | Intensity | No. cases | Intensity | No. cases | Intensity |
| Appetite | 2 | poor | 0 | — | 0 | — | 0 | — | 0 | — |
| | 4 | fair | 0 | — | 1 | fair | 0 | — | 1 | fair |
| | 9 | good | 11 | good | 11 | good | 10 | good | 9 | good |
| Hunger-pain | 13 | 1 to 4+ | 6 | 1 to 3+ | 4 | 1 to 2+ | 4 | 1+ | 4 | 1+ |
| Belching | 7 | 1 to 4+ | 3 | 1+ | 2 | 1+ | 1 | 2+ | 1 | 1 to 2+ |
| Heart-burn | 2 | 1 to 3+ | 3 | 1 to 2+ | 0 | — | 0 | — | 0 | — |
| Nausea | 3 | 1+ | 1 | 1+ | 2 | 1+ | 0 | — | 0 | — |
| Vomiting | 3 | 1+ | 0 | — | 0 | — | 0 | — | 0 | — |
| Abd. pain | 10 | 1 to 4+ | 4 | 1 to 3+ | 2 | 1+ | 0 | — | 1 | 1+ |
| Diarrhea | 1 | 1+ | 1 | 1+ | 2 | 1+ | 0 | — | 0 | — |
| Constipation | 6 | 1 to 4+ | 7 | 1 to 4+ | 3 | 1 to 2+ | 3 | 1+ | 2 | 1 to 4+ |

c) Three patients continued to present x-ray evidence of active ulceration but less active than before treatment was started.

Case 14 was a known peptic ulcer patient for 5 years. At the 28th week of treatment x-ray revealed that the ulcer was still slightly active. At the 40th week the patient had a cholecystectomy and the surgeon reported that the ulcer was healed. The patient has been asymptomatic since that operation.

The last two cases had their ulcers for 2 and 24½ years. At the end of 26 weeks and 6 weeks respectively the ulcers were still slightly active.

## Comparison of Final Effects

The diet used in each of the studies, the effects of which are to be compared, was the same. The criteria used for comparison are the effects on weight change, constipation and x-ray changes.

The findings were as tabulated below:

| Treatment used | Constipation (No. of patients) | | Average of those gained wt. | X-ray (Inactive or no ulcer) |
|---|---|---|---|---|
| | Before | Final | | |
| (a) 15 patients from 6 through 40 weeks | 6 | 2 | 5.72 lbs. | 80% (12 patients) |
| (b) 18 patients from 6 through 50 weeks | 10 | 1 | 7.22 lbs. | 83% (15 patients) |
| (c) 20 patients from 6 through 12 weeks | 7 | 7 | 2.5 lbs | 40% ( 8 patients) |

(a) =combined protein hydrolysate and nonreactive aluminum hydroxide gel.
(b) =protein hydrolysate, daily one ounce per 50 lbs. of body weight.
(c) =aluminum—dihydroxy—aminoacetate, 1 gram before meals and after meals and before retiring.
(a preliminary report)

These results of this investigation were evaluated against those of two other studies on peptic ulcer patients. In one protein hydrolysate was used[3]. In the second aluminum—dihydroxy—aminoacetate was under investigation[11].

## Comments

This investigator has at no time assumed that a peptic ulcer cure would thereby be achieved. Failures and reactivation of ulcers will undoubtedly be encountered. However, because an antacid with nutritive value is used in conjunction with a nonconstipating antacid, this treatment merits consideration, and further investigation. The routine administration of the medicaments being given at such times that the ulcer symptoms are anticipated further recommends this treatment. Regardless of symptoms, *every* ulcer treatment should be continued for about two years and the patient x-rayed periodically.

## Conclusions

1. As a rule large doses of protein hydrolysate to supplement the protein absorbed from peptic ulcer diets are not necessary.

2. At the end of about one hour the antacid effect of protein hydrolysate ends and it then has a gastric secretagogue effect. This is controlled by the nonreactive aluminum hydroxide gel mixture that is given according to the recommended routine.

3. No laxatives are needed since constipation is eliminated in most cases. This troublesome symptom is frequently encountered in ulcer patients and not infrequently is aggravated by other treatments.

4. The symptoms were quickly controlled and remained controlled throughout this study. The administration of the medications was timed in anticipation rather than development of symptoms.

5. The patients' general conditions were markedly improved.

6. There were no untoward effects.

7. The 80 per cent x-ray evidence of inactivation or nonvisualization of the ulcers in asymptomatic patients is quite high.

8. The medications and routine are only recommended as a worthy measure in the treatment of peptic ulcer patients and not as a cure.

9. The results indicate that this routine of treatment merits further investigation.

The author wishes to express his thanks to Marvin R. Thompson Inc., Stamford, Conn. for the protein hydrolysate and to the William R. Warner Pharmaceutical Co., New York, N. Y., for the nonreactive aluminum hydroxide gel mixture used in this investigation. An expression of gratitude is hereby extended to Dr. Sarah E. Worob, Miss Renee M. Ailion and Miss Helen Sharkin for their cooperation in the management of the patients and their aid in coordination of this paper.

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# SURGICAL THERAPY IN GASTRODUODENAL ULCER*

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The recent and accurate observations of Dragstedt strongly suggest that an excess of unneutralized and undiluted gastric acid is a most important factor in the etiology of peptic ulcers. Pure gastric juice differs from gastric contents in that the latter is a mixture of the former plus saliva, food, mucus, regurgitated duodenal juices and a neutral or faintly alkaline secretion from the pyloric antrum; this was demonstrated in animal experimentation with Heidenhain or Pavlov pouches. Whereas pure gastric juice may be detrimental to living tissue, gastric contents are almost entirely inert. Brodie[1] in 1814, observed that the stomachs of dogs filled by intravenous injections of arsenic contained large amounts of mucus and watery fluid; if, however, the vagi were cut prior to the administration of arsenic, the stomach remained empty, therefore, the effect of section of the vagus nerves on gastric secretion is not new. In 1870, Wood[2] confirmed these observations. Pavlov[3] in 1894, made similar observations on dogs and found that hydrochloric acid was not present following section of the vagus nerves. Further work by Pavlov[4] in 1910, emphasized the nervous or neurogenic factor in gastric secretion, which he thought could be completely abolished by vagus section. His deductions were only partially correct, since A. J. Carlson[5] has shown that although the nerve or neurogenic secretion was abolished, there still existed a hormonal (humoral) secretion (gastrin), which is believed to be formed in the intestine and absorbed by the blood stream. When food is present in the stomach, this secretion is formed even though the vagi are cut. The amounts of secretion produced by neurogenic and hormonal stimulation is unknown. Ivy[6] (1925), and Lim, Ivy and McCarthy[7] (1925), have made valuable contributions to this subject and have confirmed the work of Pavlov. In 1901, Bickel[8] removed the duodenum in two dogs and re-established continuity by means of a gastrojejunostomy. The bile and pancreatic ducts were implanted into the anterior abdominal wall. Four and one-half weeks later, an autopsy revealed that one of the animals had developed jejunal ulcers, one of which had perforated, producing a peritonitis and death. The rarity of spontaneous ulcer in the dog has been recognized by a number of investigators[9, 10, 11] therefore, dogs are usually chosen as the laboratory animals for these experiments[12]. In 1911, Exalto[13] noticed that no ulcers developed in dogs in which a gastroenterostomy was performed, but were frequently noted in those animals in which he did a Roux "Y" operation. He concluded that jejunal ulcers were due to acid gastric juice acting upon the intestinal mucosa. Mann and Williamson[14] described an operation in which the alkaline duodenal contents were shunted into the terminal ileum, and fourteen of sixteen dogs upon which they performed

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this procedure developed jejunal ulcers. Neuman, Demoor and Deloyers[15] found ulcers in four of seven dogs who had a shunting of their bile into the terminal ileum, and Berg and Jobling[16] produced chronic duodenal ulcerations in thirteen of twenty-three dogs following various types of biliary exclusions.

In 1931, Elman and Hartman[17] produced ulcers in six dogs with pancreatic fistulae and emphasized the importance of pancreatic juice. Berg[18], however, was able to produce only one ulcer in sixteen dogs with pancreatic fistulae, and no ulcers following total pancreatectomy in eight additional dogs. Kim and Ivy[19] experimenting with neutral gastric mucin noted spontaneous duodenal ulcers in six of ten dogs with biliary fistulae.

Matthews and Dragstedt[20] reviewing the work of Dragstedt and Vaughn[21] emphasized the importance of the neutralizing effect of saliva, food, mucus and duodenal juices. Ochsner, Gage and Hosoi[22] were able to produce ulcers in 85 per cent of animals in whom gastric pouches were anastomosed to the jejunum, however, if bile was introduced by anastomosing the gallbladder to this pouch, the incidence of ulcer dropped to 39 per cent. DeBakey[23] also attempted to answer the perplexing question, namely, which had the greatest protective power, bile, pancreatic juice or succus entericus. He did this by performing gastrojejunostomies with Von Eiselsberg[24] pyloric exclusions, and then excluded bile and pancreatic juice separately and collectively. He found with pyloric exclusion alone, 50 per cent of the animals developed ulcers; with pancreatic juice excluded, 70 per cent; with bile excluded 90 per cent; with both juices excluded, 100 per cent. He concluded that bile was of the greatest importance in preventing jejunal ulcer formation, pancreatic juice next and succus entericus least. In 1941, Varco, Code, Walpole and Wangensteen[25] produced increased gastric secretion and ulcers by intramuscular injection of histamine-beeswax mixture in dogs.

In 1925, McCrea[26], after reviewing and studying the subject came to the following conclusions: unilateral vagotomy did not affect the motor activity of the stomach and bilateral vagotomy merely decreased the initial emptying time. Section of the vagi eliminated the psychic secretion, but the chemical phase of secretion still persisted. In 1929, Hartzell[27] reported that following transthoracic vagotomies on dogs, complete section of the nerves induced a decrease in acid secretion; transabdominal vagus section showed no constant decrease in the height of acid. If the vagotomy was incomplete, no decrease in acid secretion resulted.

In 1930, Dragstedt and Ellis[28] in an attempt to secure information concerning the relative importance of the vagus nerves in the secretion of gastric juice, performed an experiment with dogs in whom they isolated the stomach (nerve and blood supply intact); intestinal continuity was made possible by an esophagojejunostomy. A gold plated cannula placed in these stomachs collected the secretions. After eating, the isolated stomach secreted from 1,000 to 2,500 cc. of highly acid gastric juice in a twenty-four hour period. The animals would have to be kept alive by supplying them with chlorides, since they would "secrete themselves to death". Those dogs which were kept alive developed ulcers. If the vagi were cut, the acidity

and amount of secretion immediately dropped to 300 to 600 cc. per twenty-four hours, and ulcers did not develop[29]. These theoretical considerations led Dragstedt to attempt section of the vagus nerves as a treatment for peptic ulcer.

In 1914, Exner and Schwarzmann[30] performed subdiaphragmatic resection of the vagus in patients suffering with gastric crises, and by adding a gastrojejunostomy they attempted to avert the effects of atony, dilatation and pylorospasm. In 1920, Stierlin[31] was the first to suggest an operation on the nerve apparatus of the stomach for ulcer cases in humans. His operation consisted of a circular incision through the muscularis and to the submucosa on the upper part of the corpus of the stomach; this incision was then sutured together. By this procedure, he proposed to cut the nerves, but Stierlin's circular myotomy failed because of an erroneous conception of the anatomy of the vagus nerves. Latarjet[32] in 1921-1922, devised an operation, vagotomy plus gastroenterostomy, in which he attempted to remove sensation, diminish the frequency and intensity of the contractions, and to diminish acidity. Schiassi[33] in 1927, also attempted to cure ulcers by nerve section, and obtained favorable results in a group of twenty-five patients. Alvarez[34] (1928), lowered gastric acidity following experimental vagotomy.

In 1938, Winkelstein and Berg[35] reported that vagotomy alone or in combination with other surgical procedures seemed highly desirable in the therapy of peptic ulcer. In 1944, Weinstein, Colp et al[36] while writing on vagotomy in the therapy of peptic ulcers, stated that "in none of the cases was clean cut evidence of beneficial therapeutic effect obtained".

In 1932, Cushing[37] stressed the importance of the part played by the central nervous system on the pathogenesis of ulcers. In this modern era of psychosomatic medicine, the importance of nervous tension, emotion, stress, strain, responsibility, competitive effort and frustration have all been emphasized. Winkelstein[38] has presented evidence that the hypersecretion of gastric juice in ulcer patients is of nervous origin, and that subphrenic section of the anterior vagus nerve together with partial gastrectomy or gastroenterostomy lessens ulcer recurrences. The central nervous system may cause ulcers by producing a hypertonus in both the secretory and motor fibres of the vagus, hence, severing them seems logical. Both hypermotility and hypersecretion are abolished by complete section of the vagal fibres[39], and the secretion and acidity tend to return to normal. Between meals, when there is no buffer action of food, hypersecretion and hyperacidity may prove dangerous. At the present time, Dragstedt[29] has obtained beneficial effects with vagotomy, and to date has reported no ulcer recurrences, however, he states that "a longer period of observation and a more extensive series of patients are obviously necessary to provide final answers".

## Anatomy

Complete severance of the vagus nerves is necessary to successfully correct hypersecretion and hypermotility. To accomplish this it is necessary to thoroughly understand the anatomy. Unfortunately, there are marked contradictions in our

leading anatomy text books regarding the vagi. This is probably due to the fact that erroneous information was obtained from the works of Hirschfeld-Leveille[40], and Kollman[41] in the middle of the nineteenth century, and many of our modern textbooks have obtained their information from these sources.

E. Perman[42] provided the most reliable information on this subject. In 1935, he performed a series of painstaking and accurate dissections dealing with the vagi. His conclusions are interesting, instructive and apparently accurate. He states that both vagi reach the stomach through the lesser omentum, and that they divide into branches without the formation of a plexus of intertwining fibres. He demonstrated that anastomoses exist between the various branches, but that they do not lose their individuality as would be the case in a nerve plexus. The *left vagus nerve* sends branches to the liver and to the anterior wall of the stomach. Those traveling to the liver turn to the right, pass through the lesser omentum and to the porta hepatis. The gastric branches divide into several smaller nerves, which spread over the anterior wall and can be followed to the greater curvature. The *right vagus nerve* is arranged in a similar manner; one part to the celiac plexus, and the remainder supply the posterior wall of the stomach. Perman was unable to follow branches of either the left or right vagus into the greater omentum.

Recent studies dealing with the subject of the nerve supply to the stomach are also quite contradictory. Bradley, Small, Wilson and Walters[43] examined one hundred and eleven cadavers, and concluded that there was a great variation in nerve pattern from the cardiopulmonary plexus to the stomach, but the nerves were very constant in course and distribution after reaching the stomach. They divided the nerve patterns into four groups. Miller and Davis[44] studies the vagus nerves below the level of the pulmonary plexus in thirteen cadavers. They state that in only three instances were the nerve arrangements comparable to those described in the text books as "normal", and the remaining ten showed marked variations.

## Transabdominal Versus Transthoracic Vagus Nerve Section (Vagotomy)

Walters et al[43] state that in 90 per cent of cases a transabdominal subdiaphragmatic approach will allow as nearly a complete division of the gastric nerves as the transthoracic route. Miller and Davis[44], however, are of the opinion that the transthoracic approach is the one of choice.

Each of the approaches have their advantages and disadvantages. The *transthoracic approach* has the following advantages:

(1) Good exposure.

(2) More complete sectioning of the nerves.

Disadvantages:

(1) The lesion cannot be examined (possible malignancy).

(2) Pyloric obstruction cannot be corrected.

(3) Postvagotomy gastric atony cannot be corrected.

(4) Postoperative pain in the incision and costovertebral joint may result.

(5) Gastroenterostomy is a difficult and unsatisfactory procedure when performed as a secondary operation upon a dilated and atonic stomach.

(6) Intrathoracic complications may result.

Keeping the above facts in mind, it becomes apparent that each case will present a problem unto itself, and that it will be up to the surgeon's judgment and evaluation to decide which of the two approaches is preferable. For example: it is still a fact that every gastric ulcer is a potential malignancy. Warren H. Cole[45] states that gastric carcinoma is preceded in from 5 to 10 per cent of instances by an ulcer. Such lesions, therefore, should be exposed, removed and examined, whether or not vagus nerve section is performed. It would be a gross error to believe that one has done a complete bilateral vagus section only to learn later that some of the vagal fibres have remained intact and a gastric carcinoma developed. The transthoracic approach, on the other hand, is indicated for duodenal ulcers, especially if a previous gastroenterostomy has been done; this approach is also excellent for anastomotic ulcers if it is deemed unnecessary to remove the ulcer. At present, the transabdominal route is favored for the reasons cited above, and especially since a gastroenterostomy may be done simultaneously to compensate for the atony which may result following the section of the nerves. Such atony is no true paralysis, but may result in an acute dilatation of the stomach brought about by the release of the hypertonicity plus swallowed air, saliva and mucus. In our series, seven cases were done transthoracically and the remaining fifty-six transabdominally.

## Surgical Technic

*Transabdominal Vagotomy*:—A long incision is necessary to obtain proper exposure. We utilize a left muscle-splitting rectus incision which commences in the angle between the xiphoid and left costal cartilage and extends one or two inches below the umbilicus. The peritoneal cavity is entered and the left triangular ligament of the liver is exposed and made taut. This bloodless fold is incised and it then becomes possible to retract the left lobe of the liver to the right. The peritoneum covering the lower end of the esophagus is incised and a finger or scissors is placed into the posterior mediastinum to mobilize the esophagus so that its lower three or four inches can be delivered into the abdomen. The nerves are treated in much the same way as will be described in the transthoracic procedure: at times it is possible to isolate and ligate both vagi on the left side. I have observed that the left (anterior) vagus has a tendency to hug the esophagus and the right (posterior) travels a slight distance away from it; therefore, it is easier to feel and identify the latter. At the conclusion of the operation, the left lobe of the liver is permitted to fall into place; it has been found unnecessary to resuture the severed left triangular ligament. That this structure does not require suturing has been all too well revealed to the author at a postmortem examination performed two weeks following vagus nerve sectioning (case reported below). The left lobe of the liver was found firmly fixed in place. An anterior gastroenterostomy is usually

done following vagus nerve section. The suture material used in this entire series was spool cotton, the only exception being, the use of catgut in the through and through suture when a gastroenterostomy was performed[46]. These patients are placed upon no postoperative dietary restrictions whatsoever and early ambulation is encouraged.

*Transthoracic Vagotomy*:—General anesthesia with positive pressure is used, and an incision is made over the seventh or eighth rib on the left side. A large section of the rib is resected, the pleural cavity entered, and after dividing the inferior pulmonary ligament, the left lung is retracted upward. Some prefer to enter the pleural cavity through an interspace rather than resect a rib. Recognition of the socalled "esophageal triangle" aids in rapidly locating the lower end of the esophagus. This triangle is bounded in front by the heart, behind by the descending aorta, and below by the diaphragm[47]. The pleura covering the triangle is incised and the esophagus identified and mobilized. The main vagus trunks are recognized by touch rather than sight. The nerves feel like taut cords which can readily be differentiated from the more yielding muscle of the esophagus. The fibres are assembled by finger dissection into two main trunks, comprising the right and left vagi which are ligated and divided. Some prefer to take a section of the nerve, but we have not done this routinely. In addition to the two trunks, small vagal fibres penetrate the esophageal wall; these must be combed off the esophagus and severed. The esophagus is replaced in its bed, the overlying pleura sutured and the chest closed without drainage. The patients are encouraged to get out of bed the first or second postoperative day.

## Postoperative Complications

A postoperative gastric atony, not paralysis, may result. Plus a vagus and sympathetic nerve supply, the stomach has a peripheral nerve supply which gives it an automatism. In general, vagal fibres are augmentors and the sympathetic fibres decrease tonus. Postvagotomy atony is believed to be due to a transient increased pyloric tonus; swallowed air and saliva may aggravate the condition so that an acute gastric dilatation results. To prevent this, constant Wangensteen suction is instituted for three to five days postoperatively. This is continued until all tendency to develop nausea or vomiting is relieved. Certain medicaments, especially those of the choline group, show some promise in the treatment of gastric atony; time will prove their efficiency. A certain number of patients have a tendency to contract diarrhea, but this has not proved annoying and has been only transient. Three patients in my series stated that a very resistant and annoying chronic constipation was completely relieved after vagotomy. Foul smelling belching and emesis may result; we have not noticed these complaints. In this series no esophageal spasm was noted.

One of Dragstedt's patients developed a postvagotomy obstruction, which was thought to be due to the vagus nerve section. However, upon reoperation by Warren H. Cole[48], this was found to be due to cicatricial stenosis caused by a healing ulcer.

To obtain complete relief and successful results, it is imperative that all vagal fibres be severed. Many tests have been devised to determine whether or not this has been accomplished, but the two most commonly used are the sham meal and insulin tests[49]. Since insulin-shock complications are always a possibility with the insulin test, it is essential to have a doctor present for the immediate administration of glucose.

That it is possible to overlook fibres of the vagus nerve seems to be agreed. Dragstedt states that in his first fifty transthoracic vagus nerve sections, three incomplete vagotomies resulted. Hollander reports that in a series of twenty-one cases, forty-eight per cent proved to be incomplete with the insulin test[50]. It must be remembered, however, that gastroenterostomy or gastrectomy also reduce gastric acidity, hence, when these tests are performed in connection with vagotomy, it may be difficult to tell which procedure is responsible for the resulting achlorhydria.

## Personal Observations

To date the author has performed sixty-three vagotomies in the past two and one half years; three deaths are recorded in this series, none of which can be directly attributed to the operative procedure. The first of these patients developed a gastric dilatation. This was believed to be due to the bilateral vagotomy, but postmortem examination revealed that the main trunk of the right (posterior) vagus was completely missed and remained intact. A massive left lobar pneumonia accounted for the demise. The second death was in a patient who had a gastroenterostomy seventeen years prior to entrance. He entered with a diagnosis of a marginal ulcer. A degastroenterostomy was performed followed by a subtotal gastric resection. Six weeks later, he was readmitted to the hospital with violent pain. Exploration revealed three new acute jejunal anastomotic ulcers. A more radical resection was done and transabdominal bilateral vagotomy added. He obtained immediate relief and left the hospital in two weeks. Seven weeks after the operation he was rushed to the hospital in a state of profound shock with signs of a generalized peritonitis. He expired and postmortem examination revealed a ruptured jejunal ulcer. The third patient expired forty-eight hours following a bilateral transabdominal vagus section and anterior gastrojejunostomy. Shortly after surgery she developed a shock-like syndrome from which condition she did not recover. Permission for autopsy could not be obtained, hence, no conclusions can be drawn. When analysing these three patients, the immediate cause of death could not be blamed directly to the vagus nerve section.

Weeks, Ryan and VanHoy[51] reported two deaths associated with supradiaphragmatic vagotomy, but since one of these was associated with a bilateral thoracolumbar sympathectomy, and the second patient had a known methyl alcohol poisoning, and at that only had the right vagus sectioned, it is difficult to see why the vagotomy per se should be blamed.

In our remaining sixty cases, the results have been most encouraging. It is indeed gratifying to note the immediate relief obtained following vagotomy, and the ability of the patient to again enjoy a full meal and lead a normal life. Moore

et al.[52] recently reported a series of forty patients upon whom he performed resection of the vagus nerves. The authors stated that their clinical results were good and that healing of the ulcer was the most uniform feature; transient undesirable side effects were found in about 10 per cent of the patients.

What the future holds for the functions of the liver, pancreas, kidney and intestinal tract following vagus nerve section cannot be stated at this time. However, since the author's last report[53], he is still as enthusiastic about the procedure. Although these pros and cons cannot be definitely answered, the questions should be approached and followed with an unbiased attitude. Whether or not the vagus nerves will regenerate can only be proven by careful "follow-ups" of these patients.

## Summary

1. A personal series of sixty-three cases is reported and three deaths in this series evaluated.

2. The transabdominal approach has distinct advantages in that the lesion may be inspected and a gastroenterostomy performed to compensate for obstructive or atonic complications.

3. If the divided vagi will regenerate or if permanent impaired gastric motility will result cannot be stated at this time.

4. The operation seems indicated in duodenal and stomal ulcers which do not respond to medical treatment. Gastric ulcers with their probable tendency toward malignant degeneration should be resected.

5. Vagus nerve section, may one day have a definite place in the therapy of peptic ulcers, however, the period of observation has been too short for final deductions.

6. The literature pertaining to vagotomy and peptic ulcer has been reviewed.

## Addendum

Since this paper was presented, an additional 47 vagotomies have been performed; the results are still most encouraging.

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## Discussion of Symposium on Gastroduodenal Ulcer

*Dr. David Adlersberg (New York, N. Y.):*—Dr. Allen's paper is an important contribution to an important topic. It is the problem of gastric ulcer in its relation to gastric carcinoma. We are all familiar with the sad state of affairs regarding the therapy of gastric carcinoma. Despite all modern technical advances, the diagnosis of gastric cancer is often made at a time when the lesion is too far advanced for surgery; thus, the results of surgery of gastric cancer are discouraging. That is why Dr. Allen's paper is so vital.

Dr. Allen stresses the importance of early diagnosis and I think that everybody will agree with him that all of us—and I purposely repeat it—should lend our influence to outlaw insidious advertising in the press and on the radio in regard to the remedies purporting to relieve acid indigestion. We so frequently see patients with a serious gastric disease who have been treating themselves with all kinds of medicines which they purchased because of radio or newspaper advertisements.

We learn that about 14 per cent of cases diagnosed as gastric ulcer prove to have cancer on pathologic, and especially histologic, study. I am happy to see that this figure is only 14 per cent—and in a recent study of another distinguished Boston investigator, Dr. Sara M. Jordan, it was only 12 per cent—because you may recall that only a few years ago some observers were convinced that this figure may be as high as 40 per cent.

Now, on the other side of the ledger, we see that 5 per cent of patients who had the preoperative diagnosis of gastric cancer, proved to have gastric ulcer. Here one must also add cases diagnosed as cancer, which, at operation, were found to have no pathology at all or to have hypertrophic gastritis.

These errors in diagnosis occur in the best hospitals of the country and cannot be prevented by all modern aids in diagnosis. Dr. Lahey states in one of his papers, that his conscience is satisfied even when after gastric resection the stomach suspected of having gastric carcinoma, proves to have only antral gastritis.

Because of all these difficulties, Dr. Allen is of the opinion that one should be extremely cautious in advising conservative therapy in gastric ulcer.

Dr. Allen wisely discusses the differential diagnosis of gastric ulcer and cancer: The location of the lesion, the size of the ulcer, the age of the patient and other criteria. Important as they are, they are of little value in the individual problem-case. It is of little help in the individual case to know that 65 per cent of the prepyloric lesions are usually neoplasms, or that 30 per cent of the lesions in patients who have had their ulcer for over 5 years after the age of 45 are benign ulcers, for if your patient has a malignancy, he has it 100 per cent and regardless of his statistical expectancy. As a matter of fact, in my opinion, some of the data even may be misleading because of our tendency to neglect signs or symptoms of lesser statistical importance. Nevertheless, for scientific reasons, we must evaluate statistically both our diagnostic armamentarium and the therapeutic results.

We agree with Dr. Allen that in a certain group of patients with gastric ulcers, differential diagnosis from early carcinoma is impossible. When all diagnostic efforts prove inconclusive, surgical exploration is indicated. Surgery is also indicated in all cases of gastric ulcer which do not heal completely under conservative treatment. To an internist, Dr. Allen's conclusion that *all* patients with gastric ulcer should be treated by partial gastrectomy appears too radical and not warranted by his own clinical experience. Surgery for gastric ulcer should consist of resection of the stomach; vagotomy has no place because an anastomotic ulcer rarely follows "adequate resection for gastric ulcer".

Finally, I wish to take exception to another statement of Dr. Allen's and that is that the results of surgical treatment in benign gastric ulcer may be better than conservative therapy. They may be better, but they also may be worse. I am referring to a group of patients who, after gastric resection, present very undesirable sequelae in absence of an anastomotic ulcer. We proposed the term "postgastrectomy syndrome" to characterize this clinical entity (Surgery, **21**:720, 1947). Of all patients who had partial gastric resection for ulcer, approximately 15 per cent present the "postgastrectomy syndrome". They are unable to gain weight and to work, they complain of dizziness, fullness, pressure, nausea, belching and a tendency to vomiting during and shortly after meals, and of headaches, fatigue, weakness, palpitations and perspiration 1-2 hours later. The "early" postprandial symptoms compel these patients to consume only small amounts of food, while the relief of the "late" symptoms by eating teaches them to take food at frequent intervals. There is often a conflict between the fear to eat and the necessity to relieve the "late" symptoms by eating. Thus, these patients present very difficult clinical, nutritional and psychological problems. It is fortunate that they represent only a small percentage in comparison with all those who are really benefited by partial gastrectomy for peptic ulcer.

*Dr. Phillip T. Knies (Columbus, Ohio):*—It will not require five minutes to agree with Dr. Allen. One point of Dr. Allen's paper I should like particularly to emphasize, namely that in certain cases one should reserve the right to judge between conservative and surgical therapy of gastric ulcer. With small ulcers in the safer zones of the stomach, one is warranted in carrying out medical treatment, while with large ulcers or the less favorable zones of the stomach surgery becomes practically mandatory.

Dr. Allen has pointed out the importance of early decision in this respect rather than reliance on prolonged medical management before concluding a lesion is malignant. Unfortunately I cannot always feel completely confident in a very early decision. For this reason, and in frank admission of possibilities contrary to one's judgment of benignity of a lesion, it becomes important to follow such lesions by frequent re-examination, by whatever means appear most critical. I have frequently been impressed with the critical variation in findings by the same roentgenologist on serial examinations. Thus it seems inadvisable, especially when there has been any question, to accept as final a single opinion of benignity.

One is, of course, obligated to act decisively when the roentgenologist has felt justified in diagnosing malignancy, but when a gastric lesion has been considered benign one must, in view of Dr. Allen's figures, re-examine the individual until all reasonable doubt is eliminated.

The same pertains to gastroscopy. With prepyloric lesions, of which 65 per cent are malignant, and with those on the lesser curvature of the stomach, of which only 10 per cent are malignant, one often deals with either a blind zone on gastroscopy, or with the ability to view the lesion only tangentially. Technical advances may permit more adequate visualization, but unless the gastroscopy is effective in demonstrating the entire margin of the lesion potentially malignant, the critical examiner is obligated to repeat the procedure in hope of a more effective examination, or state that gastroscopy in that instance is inadequate to be decisive. The patient cannot afford a diagnosis of benign lesion when the entire lesion has not been well seen. Under these circumstances one must again consider the statistical data Dr. Allen has presented.

*Dr. Harry Barowsky (New York, N. Y.)*:—Dr. Allen has brought to our attention a very important subject, the differential diagnosis and the disposition of gastric ulcer cases.

We all agree that it is difficult to differentiate between benign and malignant gastric ulcer; however, it is hard to agree with the speaker, who intimates that because of this difficulty, the majority of gastric ulcers are primarily a surgical problem. Gastric ulcer is relatively a common affliction, much more common than is diagnosed roentgenographically. I have frequently observed it gastroscopically as shallow, small ulcers, or ulcers of the posterior wall, and occasionally we see it at autopsy without any previous record of it. If we exposed the majority of cases with gastric ulcer to gastric resection, our total surgical mortality rates would surpass our total neglected or misdiagnosed carcinomatous ulcers.

It would be interesting to know what the incidence of carcinoma in gastric ulcer is. This information would be important to determine whether or not gastric resection should be a routine procedure in these cases.

Although the differential diagnosis between benign and early malignant ulcer is extremely difficult and at times impossible, I have brought to your attention in previous publications certain criteria which I have observed gastroscopically, which have proved very helpful to us. It is true that where the ulcer is not seen, we cannot make a diagnosis, but, where it is seen, we have certain criteria which I should like to stress.

First, the site of the ulcer. In benign peptic ulcer, it is situated on a flat surface. Carcinomatous ulcer is usually situated on an elevated area. Second, in shape, it is deep, punched out, and crater-like in appearance when benign, and frequently it is bowl-shaped and shallow in a malignant ulcer.

Third, the margin is well defined in its entire circumference in benign lesions. In malignant lesions it is round, sloping, and generally does not form a complete circumference. It may be lost in the adjacent tissue.

Fourth, the floor of the ulcer and its color—the floor is a gray tone, to a whitish yellow, occasionally brown, and, after a hemorrhage, dark red, but usually gray and whitish yellow in benign ulcer. In malignancy the lesion, the floor, rather, may be of many colors, usually appears necrotic, and is dark brown or dirty gray in color.

Fifth, the floor, its structure—the floor is generally even and flat, sometimes smooth, in benign lesions. In malignant lesions the floor is irregular, nodular, and has ridges, pieces of necrotic tissue which may be observed occasionally.

Sixth, we have the surrounding area—the surrounding mucosa ordinarily is normal. Sometimes it may be inflamed; however, it is always flexible in benign lesions. In malignant lesions the surrounding mucosa in advanced stages is sometimes nodular and appears stiff and infiltrated. Its color is at times a pale red.

These criteria are present, of course, in the classical benign and the classical carcinomatous ulcer. It is my impression that when any of the malignant criteria are observed, the patient should be referred for surgery.

In conclusion, I wish to emphasize that although a great deal of difficulty is encountered in differentiating between benign and carcinomatous ulcer in the early stages, the more advanced cases can be diagnosed if they are properly observed.

In our institution we have set certain criteria for surgical resection and they are:

1. Those gastric ulcers which do not heal readily.
2. Those ulcers which have a tendency to recur or become chronic.
3. The recurrent or poorly controlled hemorrhagic ulcers.
4. Gastric ulcers situated on the greater curvature of the stomach.
5. When any malignant criteria are observed either roentgenographically or gastroscopically.

*Dr. Dwight T. Bonham* (*Hempstead, N. Y.*):—I heartily agree with Dr. Rivers that it is impossible to universally apply any régime in the therapy of peptic ulcer. A variety of measures has been introduced to treat the ulcer patients, including many kinds of parenteral adjuvants, the drip treatments, and gastric mucin, in addition to the modified diet program with alkalis, antispasmodics, and sedatives. All of these may be used in the treatment of the intractable ulcer; however, we must consider it is more likely that the patient is intractable. This, I feel, is a point we very frequently forget and, along with Dr. Rivers, we probably must realize that the tensions in these intractable ulcers originate in the cortex in most of these people.

This makes us aware of the problem noted by Dr. Rivers, that a régime must take into consideration general and individualized etiological factors.

I was sorry that Dr. Rivers did not make some comment, or perhaps he might make some comment upon his work at the present time with hormone therapy, or whether they are doing anything of that sort, in view of his original

work with enterogastrone. I have not had the privilege of working with hormone therapy, using upon patients enterogastrone and urogastrone and allone, which is considered as an anti-ulcer factor. Undoubtedly these or other similar-acting hormones will, with a better understanding of the complex glandular reaction, prove to be a major factor in understanding the histopathological state of the peptic ulcer in the individual case.

I feel that we are all aware of the role that nutrition plays in the ulcer patient, both as to the adequate protein and adequate vitamin content of the diet.

A number of points were brought out by Dr. Rivers in his paper this morning as to the erosion factor, the acid erosion factor, the constitutional diathesis, and, above all, the accuracy in diagnosis. I think we enjoyed his grouping of syndromes in studying the ulcer problem.

As to his treatment, the medical treatment, or whether it should be surgical, I feel that that is pretty generally the same for all of those working in gastroenterology.

It has been a privilege to hear this well-developed and orderly presentation by Dr. Rivers upon this most important subject of the therapy of peptic ulcer. He has convinced us that ulcer therapy must be tailormade for the case, depending upon the histopathology of the lesion and the etiological factor as best we may know it today as being important for that case.

I am sure that we have indeed enjoyed your paper, Dr. Rivers, and I am certain that those of us in actual practice who have had little experience with the problem of hormone therapy would like to hear from you on that subject.

*Dr. Herbert L. Weinberger (New Orleans, La.):*—Dr. Rivers presented in his paper the five productive criteria of ulcer, that is, its definition from the standpoint of:

1. Visceral ulcer syndrome without referred pain. This type of ulcer we consider to be entirely medical from the standpoint of treatment.

2. Visceral ulcer syndrome with referred pain. He considers this type the multiple ulcer for which medical treatment may be instituted. With this, I understand, it may be the intractable ulcer that we see as a surgical problem.

3. The perforating peptic ulcer syndrome with admixture of visceral and somatic pain may be given a test medical treatment, but usually ends up with surgery.

4. The perforating ulcer syndrome referring with replacement of visceral and penetrating ulcer inflammation is also a surgical problem.

5. The ulcer group with phrenic radiation following penetration, and abscess formation is a surgical problem.

The many failures of medical treatment, in my opinion, are due to insufficient treatment. In most instances we treat the ulcer patient too lightly due to the fact that he is so easily relieved, and thus he is so easily neglected. The end result

is that the symptoms are relieved, but the complex mechanism which produced the ulcer is not given consideration.

The socalled ulcer diathesis case is something that seems to be beyond the pale of just simple medical régime. It is a question of psychiatric analysis, whether informal or formal, depending upon the case.

So far as the methods of treatment empirically, in those selected cases (so-called uncomplicated duodenal ulcers), I have had some experience with the use of enterogastrone. At the present time I believe in our hands enterogastrone has been no better than the usual methods we have employed, that is frequent feedings, and the usual aluminum hydroxide substances.

In the cases of intractable pain, that is, the hypersecreting ulcers (in which we have our severe pains at night), we have gone to the continuous intragastric drip. In these cases we do not use continuous drip, but we use our drip at night, and during the daytime we use the conventional frequent feedings and an aluminum hydroxide.

We have been playing with the protein hydrolysates and we feel at this particular point we can't agree, on the whole, with the theories that have been promulgated; that is, we do get some buffer action, but we do not find the cases of hypoproteinemia that have been found by the advocates of protein hydrolysate.

So far as the histamine treatment of duodenal ulcer is concerned, all that I can say about that would not be of much value because we have had no experience with it. I am of the opinion, considering the possible etiology, that is, the eroding factor of acid, that I would not want to use it. Inadvertently, I think I produced a case of ulcer by giving histamine.

As to the question of gastric ulcer, I think we all consider it most probably a surgical problem. We give it the test of medical treatment for a period of four to six weeks, and, if there are still some signs of the presence of occult blood, and if the x-ray evidence shows no signs of any decrease, we immediately go to surgery.

I am not in accord with Dr. Sara Jordan, in regard to the treatment of gastric ulcer. I am perfectly willing to have my gastric physiology taken away, by the surgeons, with the idea that I am able to prevent a possible malignancy.

Dr. Rivers' paper was excellent. This is the first time I had the pleasure of seeing or hearing this approach to the ulcer problem, and it certainly gives us food for thought.

*Dr. Jerome Weiss (New York, N. Y.):*—Dr. Rossien has presented some interesting facts in his paper, and these have been borne out by investigators who have studied along similar lines.

Almost similar results to those he has reported have been obtained on the Gastrointestinal Service at the New York Polyclinic Medical School and Hospital, where for some time now the treatment of gastroduodenal ulcers has been basically the same as Dr. Rossien has described. There have been some embellishments, of course, and some modifications.

The protein from which the available amino acids were obtained in this study was given in the form of a protolysate mixture which consisted of protolysate, nutramigen, sugar, and water. This made it quite palatable and acceptable to the patients. Four ounces of this mixture were given every two hours while the patient was awake, accompanied by a soft, bland diet, and two drams of aluminum hydroxide gel which was given about four times a day.

It was found expedient to give 1/200th grain of atropine sulfate at eight o'clock in the morning and again at nine o'clock in the evening to offset the marked hypersecretion, hyperacidity, and spasm which occurs. It is known that in ulcer patients this is ordinarily present and in those patients who receive hydrolysates, it is markedly increased. In the acute ulcer or in cases where there is persistent pain and the patients could not eat or refused to eat, this mixture was given through the duodenal tube with good results.

In addition to the basic therapy which Dr. Rossien described and which we followed, a synthetic formaldehyde resin in the form of a capsule or powder called "resinat" was found to have decided therapeutic advantage. Whereas with the basic therapy there was an absence of x-ray findings hunger pain, and general abdominal discomfort at the end of four weeks, with the combined therapy we were able to show negative x-ray results, loss of hunger pain, increase in weight, general improvement, within ten to fourteen days.

Two sets of x-rays were taken of patients on the service of the Gastrointestinal Department at the Polyclinic Hospital. These films, were taken only two weeks apart, and show the complete obliteration of the ulcer crater roentgenographically. Moreover, these patients felt completely well in all respects, besides being exceedingly grateful. Fortunately, the constipation was not too great a factor under the combined treatment.

I am glad that Dr. Rossien also mentioned the fact that protolysate and aluminum gel treatment should be continued beyond the stage of negative x-ray findings and the cessation of subjective symptoms. From repeated gastroscopic observation of patients who have had gastric ulcers, we have observed that long after the x-ray evidence is gone, the gastritis, which was present, still persists. As Dr. Rossien mentioned in the beginning of his paper, it is the presence of this gastritis which interferes with the proper absorption and breakdown of protein and protein products; therefore, in order to maintain the improvement through the use of this method the therapy must be continued over a period of time, from eight months to a year or longer.

That the ulcer is likely to recur is more than a possibility because we know the saying, "Once an ulcer, always an ulcer". Elaborated, it means that once a patient has shown a susceptibility to develop ulcers, he is more prone to develop new ones or break down the scar of the old one. It is also necessary to protect this patient from himself, so to speak, by maintaining him on a régime which will permit the least breakdown to his mucosa again, and therefore also his mental attitude.

Along the line of giving medication in anticipation of symptoms, and so preventing their actual recurrence, with consequent pain, discomfort, psychic upset, and reduction in food intake, either through vomiting, or nausea, or poor appetite, we have found that this clock-like method of ulcer treatment worked out very well on the Gastrointestinal Service of a large Army General Hospital of which I was in charge. The morale of the patients was very high, and the actual inbed and hospital days were reduced markedly.

Altogether this paper has brought out several points which are essential to remember, such as the importance of supplying the necessary food elements for the keeping up of nutrition where the proper absorption is impaired, supplying the adequate amounts of antacids at the proper times in order to forestall the usual symptoms, preventing many of the common side effects, such as diarrhea, constipation, or nausea, and getting the ulcer patient back on his feet in a relatively short time and, what is most important, keeping him there.

*Dr. William R. Morrison (Boston, Mass.)*:—I should first like to say I think this is a most interesting program, the most interesting that I have yet attended. This year we have heard the best men from Rochester, Chicago, New York, and my esteemed colleague, Dr. Allen, from Boston. I think this is the first time I have been at a convention where the President of the American College of Surgeons as well as a Fellow of the Royal College of Surgeons has addressed us. Dr. Allen has honored us by coming here. As you know, he is Senior Surgeon at the Massachusetts General Hospital.

I was going to say a few things about vagotomy. Dr. Thorek has read a most interesting paper. I personally prefer the transthoracic approach to take out sections of the tenth nerves. If you want to examine the lesion in the stomach, you are perfectly at liberty to open the diaphragm and take a look at it through the chest. In some of my cases I have found the lung so adherent to the diaphragm that you couldn't separate the lung satisfactorily as you went through the chest, and you had to open the diaphragm to get at it from below.

A postvagotomy gastric dilatation is usually taken care of by nature if left for months. A lot of young fellows promptly want to do a gastroenterostomy.

Dr. Max Ritvo, chief x-ray man at the City Hospital in Boston has shown in his series which he reported recently, that the gastric atony disappears as late as nine months after the operation. Postoperative lack of sensation has been noted in the incision in some of our cases. We, of course, inject pontocaine in oil in the intercostal nerve, with the idea of stopping any pain after operation.

The intrathoracic complications have not been serious in our vagotomies. To be sure, sometimes you get a little air in the chest, sometimes a certain amount of cloudiness, sometimes even a fluid level.

In my opinion gastroenterostomy is an unnecessary operation, for gastric atony following vagotomy, when the pylorus is patent. As Dr. Thorek has said, nature will close up the gastroenterostomy in about four months anyhow, if the

pylorus is patent and it is unnecessary to perform the operation under those conditions.

A section of each tenth nerve is excised for pathological report. About 70 acute perforated ulcers of the stomach and duodenum are operated on at the Boston City Hospital yearly. I have noted a good many of them that perforated the second year, several the third year in succession, and one four years in succession.

I should like to ask Dr. Thorek and Dr. Allen if they feel that they would resect the stomach at the second perforation or at the third or fourth perforation.

I have noted in some of the cases that I have worked up for vagotomy that before I could get around to operate on them, the ulcer would perforate. It doesn't mean that if you have done a vagotomy in that case, and it perforates a day or so afterwards, your vagotomy has anything to do with it. If the ulcer is about ready to perforate, it would probably do so anyhow, whether you did your vagotomy or not.

Now, another thing—the x-ray expert may tell you that a stomal ulcer is present, and he shows it to you in the x-ray, then you have one of your men gastroscope the case. McClure and Jankelson have gastroscoped about three thousand stomach cases at the Boston City Hospital, and we believe they are pretty accurate. Whom are you going to believe, the x-ray expert who says there is an ulcer present, or McClure and Jankelson, who may say there is nothing there?

It is possible the stomal ulcer may be down inside the jejunum where they don't see it.

*Dr. Halsey B. Loder (Boston, Mass.):*—I came here today to learn, and I have learned. I want to thank Dr. Thorek for giving as he has, a clear concrete indication for the working surgeon in the handling of the medical failures in the treatment of duodenal ulcer.

When one talks about medical failures on duodenal ulcers, remember that they are not necessarily failures of treatment method and not necessarily failures from the patient's unwillingness to cooperate.

If you stop to think of the number of men who cannot carry on in the necessary gainful occupation and take care of themselves every hour to hour and a half through the working day, you will find that it isn't always the unwillingness on the part of the patient to play ball. There are too many men with a family to support who would have to face losing their jobs, to follow through medical treatment, as I have been listening to it here this morning. Those are failures not in basic treatment, but failures from the patient's economic inability to follow treatment for six months, a year or more. They are the ones who frequently come into my hands asking for help, because they can't follow through in any other way.

Dr. Thorek has very clearly told us where to pick and choose vagotomy, which has come as an unquestionably big step ahead on our surgical treatment of the ulcers which are the medical failures.

The question of how to handle this from the standpoint of the surgeon, whose work is done in no small part in the secondary and tertiary medical centers, brings up some questions that are of practical importance to those doing that kind of work. It is one thing to do some of the gastric surgery where you have your hands on the after-care, where you have your patient more or less in the position of the patient in the investigating hospital, where the patient is more or less a guinea pig in a cage, and it is another thing to give the patient the practical relief which the patient demands, in the secondary or tertiary medical center. These things do have to be simplified, and it does bring to me a question I should like to ask of Dr. Thorek: whether he has any failures to report in his subdiaphragmatic vagotomies.

As I have listened to and watched the failures, they have seemed to be running to a fairly high percentage. Whether that is simply poor technic or vagaries in anatomy that can't be followed, I haven't been able to make out. It has left me with the feeling that the more certain vagotomy is the transpleural vagotomy, which is questionably to be combined with laparotomy. Certainly to reach through the diaphragm to the part of the duodenum you would want, isn't too good surgery.

I want to bring in one conception of the severe recurring ulcer, the kind that bothers the surgeon, because he can't go ahead unless he has his five quarts of blood, which he can't always have. Why does the patient have that sort of hemorrhage? I have been able to demonstrate twice at autopsy and once in a hemorrhage, that this type of hemorrhage is due to an infectious aneurysm in the pancreatic duodenal artery, and the reason for the persistence is that it is bleeding from the little intimal aneurysmal sac, the same type of secondary hemorrhage that was so common in stumps in the first world war.

So far as the surgical handling of these, there is no halfway about it. The reason I am tempted to think—I don't know that I would ever have the courage to try it—that if you opened the duodenum and simply wiped out the aneurysmal sac, thus completing the division of the vessel, just as in your palmar infected aneurysms and their hemorrhages, the hemorrhage would automatically stop.

I don't know that I would ever have the courage to do this, but it is worth a thought on this conception as to why those severe recurring hemorrhages don't behave under ordinary medical treatment or ordinary ligation.

*Dr. Hyman I. Goldstein (Camden, N. J.):*—Dr. Thorek gave us an excellent presentation on the subject. I may call your attention to his instructive and most interesting paper, which recently appeared in the Journal of the American Medical Association (**135**:1141-1145, 1947) on "Vagus Nerve Section (Vagectomy) in the Treatment of Peptic Ulcers". He has had considerable experience with vagus nerve resection for intractable ulcer. Dragstedt of Chicago (1943, 1944) has revived interest in this surgical procedure. Grimson and his associates at Duke University, Griswold and Schoen, and their associates of Louisville, Harkins and Hooker and Johns, of Baltimore, Francis D. Moore, et al. of Boston and many others, including Waltman Walters (Mayo Clinic), Ralph Colp of Mt. Sinai Hospital (New York),

and Ravdin of Philadelphia, have published the results of their experiences with "vagotomy" or vagus resection ("Vagectomy") for the relief and cure of intractable "peptic" ulcer. It appears to us medical men that, the ultimate results and sequelae of this procedure will not be definitely known for some years and, that it is too early to state that this is now the "cure par excellence" for ulcer. My own feeling is, that marginal or anastomotic ulcer is the only real indication for "vagotomy"! It has been 134 years since Sir Benjamin Collins Brodie, in 1814, observed the prompt reduction in the acidity of gastric secretion following vagotomy in dogs. H. C. Wood, Jr. in Philadelphia, in 1870—reported the effects of vagotomy (in dogs) on intestinal motility.

Among the early workers on this problem (vagus section) were Pavlov and Schumova, Simanow-Skaja (1889), who reported the effects on gastric secretion in dogs (sham feeding) following vagotomy, and Peter Alexander Herzen (Gersten), Moscow surgeon (1897, 1898), H. Jürgens (St. Petersburg, Dissertation 1892); A. Latarjet and P. Wertheimer (Lyons, France), W. B. Cannon (1906), Vanzant (1931, 1932), Wilhemj et al., Hartzell, Gino Pieri and Lapenna & Tanferna, F. Högler (1933), Eugene Klein (1929), Ralph Colp, and many others.

Of interest, is the published work of Gino Pieri, Italian surgeon of Rome. Pieri and his associates did both transthoracic and transabdominal vagotomy for the cure of ulcer (1927, 1930, 1932). The acid factor in relation to "Peptic" ulcer has been suspected, and known, since the time of Celsus (53 B.C.-7 A.D.?) antacids and adsorbents have been used for centuries in the treatment of peptic ulcer by Aëtius, Paul of Aegineta, Hernius (van Heurne), Riolan, Scultetus, the great Spigelius, and by Sir Gilbert Blane (1796). Blane in 1796, stated that alkalis, magnesia, calcareous earths, kaolin (aluminum silicate or terra sigillata) markedly reduces acid gastric secretion—this was in 1796—28 years before Prout (in 1824) discovered hydrochloric acid in the gastric juice! Blane's treatment (1796) was somewhat similar to Rivers' (Mayo Clinic) "cocktail" for hyperacidity!

Russell S. Boles, of Philadelphia, in his paper on "Modern Medical and Surgical Treatment of Peptic Ulcer" erroneously states "In 1793 Matthew Baillie of London, described morbid anatomy and symptoms of ulcer of the stomach. The *first* reference in medical literature to ulcer of the duodenum appeared in 1817 in the London Medico-Chirurgical Transactions". (Mr. Travers' report of two cases of perforation). He then refers to Bucquoz' report (1887) of five cases of duodenal ulcer, and Cruveilhier's principles of medical treatment of ulcer. Boles was unaware of Galen's quotation from Diocles' (350 B.C.) description of symptoms and the writings on "ulcera stomachi" ("ulcus ventriculi") of the ancients, and those of the middle ages—and the reports by Blane, Jacopo Penada (1793), and the "ulcer lives" of Cardinal Caesar Baronius, who died of "ulcera stomachi", (proved at autopsy) on June 30, 1607, ("In cadavere dissecto medici tria ulcera in ore ventriculi invenerunt, unde rebellis ejus nauseae sedatusfuit stupor"), Duchess of Orleans (1644-1670)—Henrietta Anne, who died from perforated gastric ulcer on June 29, 1670, Jean Darcet (1725-1801) noted French chemist died of perforated

ulcer (1801), Charles Darwin (1809-1882), Napoleon (1769-1821), Thomas Henry Huxley (1825-1895) and Thomas Carlyle (1795-1881) suffered from ulcer.

Rudolph Valentino died of a perforated gastric ulcer. Dr. G. Randolph Manning saw him in consultation. Cruveilheir reported the case findings (autopsy) of Jean Darcet. Jacopo Penada in 1793, reported the case of Domenico Miazzo, who died of duodenal perforation (proved at autopsy) and Donatus' patient, Camillus Facinus (Mantua) died of gastric ulcer (necropsy).

*Dr. George B. Jerzy Glass (New York, N. Y.):*—It appears from the important paper of Dr. Thorek that the vagotomy has a top-ranking place in surgical treatment of duodenal ulcer. It seems to me, however, that its physiological basis should be evaluated not only as to its effect on the gastric acidity but also on the buffering mechanism of the operated stomach. It might therefore be of some interest to discuss here the effect of the surgical procedures on the dissolved mucin of the gastric content, which seems to be involved in the maintenance of the acid-base balance of the stomach. These studies were done in the Department of Medicine of the New York Medical College by means of the recently outlined and published method for determination of the dissolved mucin by Dr. Boyd and myself (Rev. Gastroenterol. **15**:396, 511, 1948).

From our studies done in cooperation with Drekter and Heisler from the Research Unit of the New York Medical College we found that in the fasting gastric juice there is a constant deficit of mineral bases in comparison with anions. This anion surplus may vary according to the case but is always considerable and amounts in average to 23 mEq. Since no other mineral cations are available in sufficient amounts this anion surplus must be covered by nonmineral cations, i.e. by proteins among which the most important seems to be the secreted mucoprotein, which is one of the main components of the socalled "dissolved gastric mucin". If 12-16 units of insulin are injected intravenously this anion surplus increases 40 minutes after injection for about 50 per cent to the average value of 35 mEq. At the same time we find that the content of the total dissolved mucin in the stomach increased in about the same ratio of 50 per cent, i.e. in average from 190 to 310 mg. per cent. Therefore the ratio of the dissolved mucin to the anion surplus seems to remain the same before and after insulin injection which would indicate that the anion surplus is covered by the dissolved gastric mucin acting as a protein cation. This would speak for the buffering role of the mucoprotein in the maintenance of the acid-base balance of the stomach.

What is the effect of the surgical procedure upon the secretion of this product?

The curves of the concentration of the dissolved mucin and free acidity of the gastric juice before and after the intravenous injection of 12-16 units of insulin represent averages of several cases of non-operated duodenal ulcer and after subtotal gastric resection or vagotomy. It is evident that hypoglycemia and its symptoms occur about half an hour after the intravenous injection of insulin, but the acidity rise occurs later and comes to its peak at least one hour after injection only. This discrepancy in timing between the rise of the acidity and the occurrence

of hypoglycemia is due to the fact that simultaneously with the hypoglycemia there is a great rise in secretion of the mucoprotein. The acidity comes to its peak only after the concentration of the mucin decreases, so that the delay in the peak of the acidity after insulin injection may be interpreted as a result of the buffering action of the mucoprotein secreted under influence of vagal stimulation.

In the subtotally resected stomach after insulin a decreased response in acidity is noted, as compared with the non-operated stomach, but there is a tremendous rise in mucin, which is due to the fact that mucoprotein is secreted mostly by the neck cells of the gastric glands located in the fundal part of the stomach, which is not resected.

In the vagotomised stomach you will find after insulin injection a low or no rise in acidity (positive Hollander's test) and very small or no increase in dissolved mucin.

There is a similarity of the acid response to insulin in vagotomised and successfully resected stomach, and a dissimilarity of the mucin response to intravenous injection of insulin in both these conditions. This finding will give answer to the problem raised in the paper by Dr. Thorek, which I had the privilege to read in manuscript, how to tell whether the vagi were cut completely or not in cases of vagotomy associated with gastric resection or anastomosis. This question cannot obviously be answered by Hollander's acidity test since both vagotomised and resected stomach behave similarly in this respect. This is evident from the curves of acidity. In these cases the increased mucin secretion after intravenous injection of 12-16 units of insulin will prove that the vagi were not cut completely and that the low response in acidity after insulin, if present, is due to resection and not to the vagotomy. On the other hand no response both in dissolved mucin and acidity after insulin will prove the complete cutting of vagi in those cases. I suggest therefore that the mucin testing should be added routinely to the currently used acidity testing after insulin, if the evaluation of cutting of vagi nerves is requested in cases where vagotomy is associated with additional operation on the stomach, like resection or anastomosis.

The behavior of patients with the non-operated gastroduodenal ulcer and after resection or vagotomy in response to histamine stimulation is next considered. In the successfully resected stomach there is only a small increase in acidity after histamine injection. On the other hand in the non-operated ulcer, as well as after vagotomy there is a high response of the acidity to histamine. The dissolved mucin after histamine behaves in a similar manner in all three groups of cases, showing a relatively small increase in the first 20-30 minutes after histamine and a steady decrease in concentration later on.

Therefore in the non-operated ulcer, as well as in the vagotomised ulcer stomach, there is a dangerous dissociation between high response of the acidity to histamine and small response of the dissolved mucin. Since the same may appear after many other parietal cell direct stimuli, such as coffee, alcohol etc., and since we attribute buffering qualities to the dissolved mucin (at least to one

of its fractions) this may prove to be a dangerous state of affairs. In this respect the successfully resected stomach is obviously in a much better position, since the secretion of mucin is fully preserved, and the acidity is decreased both after vagal and direct parietal cell stimulation. On the other hand, in the vagotomised stomach, the mechanism of the mucin secretion is disturbed, which must impair the buffering mechanism, and the acidity is decreased only after vagal, but not after direct parietal cell stimulation.

Therefore I believe that from the point of view of the buffering mechanism of the stomach the vagotomy alone is an operation which seems to be not so perfectly motivated as it would appear from acidity studies only; if performed it should be joined to another operation on the stomach, like resection, which will decrease the acidity response not only to vagal but also to direct parietal cell stimuli.

*Dr. Henry A. Monat (Washington, D. C.):*—I listened to the discussion on ulcer all this morning and I should like to bring out certain pertinent facts which hardly ever are discussed at a meeting of gastroenterologists.

I am sure that my experience has been duplicated by others who have followed the patients carefully. Why does every one harp on controlling acidity in a duodenal or gastric ulcer?

How many of you have done the studies on ulcer cases and have been surprised that many of them did not have a hyperacidity? In my careful observations, which I had the opportunity of doing, of controlled patients in the Navy, in five hundred patients, eighteen to thirty years old, I found in only about 30 per cent of the cases with active, roentgenologically demonstrable ulcers—a rise in acidity above 50°. The majority of them, 50 per cent of them, had normal acidity curves, and 20 per cent were absolutely low.

I was also surprised when I heard Sara Jordan not long ago saying that she hasn't seen duodenal ulcer with anacidity. I saw several in my series of cases of complete anacidity with duodenal ulcer, roentgenologically demonstrable.

I also noticed that nocturnal secretion of all ulcer patients was increased. They ran to about 200 cc. about three o'clock in the morning, and it dawned upon me that their nocturnal secretion has a lot to do with their symptoms.

In the treatment, I discarded all the alkalizers, gave them milk, including one feeding at 3 a.m. They improved tremendously.

I feel that there are three points in treatment of an ulcer:

1. The control of emotional activities, which are divided into psychological adjustment of, and the social adjustment of the patient.

2. Giving patient a medical vagotomy and what I consider medial vagotomy —in form of rectal suppositories, a mixture of veronal and atropine rectally every six, or eight, to ten hours, depending on the response, until he is absolutely "gaga" —this is done from three to seven days. In the interim force—feeding them, wak-

ing them up and feeding milk, and giving a purée, a well-balanced diet from the start.

3. The feeding problem. I believe that an ulcer patient is just like a diabetic or tuberculous patient. He cannot be told six months later, "Now you can eat everything". I feel that the scar that is formed by a duodenal ulcer is a firm, fixed thing, and you have to treat it kindly throughout life, therefore I warn him that later on after the wound heals he may take bland foods, but the foods must always be mechanically, chemically and physiologically bland, and thermally neither too cold or hot. I also remind him that he must partake of foods slowly, without extraneous irritating influences such as radio, arguments, getting up from the table, etc.

*Dr. Arthur W. Allen (Boston, Mass.):*—I am grateful to you who have discussed this paper of mine; as a matter of fact, I thought it was quite provocative and I expected to get more disagreement than was shown. Obviously your Chairman picked the discussers pretty carefully.

Some very excellent points were brought out which I should like to stress. Dr. Adlersberg spoke of the fallacy of depending upon statistical data. Strangely enough, I agree with him about that although I know of no other way by which I can get a sound viewpoint about a subject that is controversial. I think we must have a base line and I know of no other way to get it except by actually evaluating what has happened to the patients who have gone through the clinic where you work.

What he really meant, and which is so important, as was also brought out by Dr. Barowsky, was that the individual consideration of each patient as a separate problem is just as important, whether you are dealing with a gastric ulcer, or, as Dr. Rivers pointed out, whether you are dealing with a duodenal ulcer.

When I first presented this statistical data of ten years ago, a great many men whose names you would know got onto the platform and said it was perfectly ridiculous, it was the most asinine thing they ever heard of, to think that gastric ulcer had to be considered in a separate category from duodenal ulcer. Those same men, now having looked up their own cases, have come around and are now just as vehement about the subject as I am.

The side effects following gastrectomy are known to every surgeon. You internists and gastroenterologists probably think you are the only people who see these poor results of the surgeon; as a matter of fact, in Boston at least, these chaps who are not happy following their surgical procedure, come back and camp on the surgeon's doorstep, and I don't mind telling you that it is a very difficult situation. Fortunately, it happens less often than we are led to believe by some papers. Also there are various ways of meeting the situation that are quite useful.

One of the most outstanding contributions to the dumping syndrome, the weight loss, and so forth, following gastrectomy, has been made by Einar Perman, of Stockholm. Shortly after and during the process of an adequate subtotal gastrectomy, it is very difficult to free the duodenum enough to bring it into contact and

approximation with the distal end of the stomach. After a certain time has elapsed, however, this segment of stomach which you have left behind has a tendency to enlarge to some extent, and the inflammatory reaction around the duodenum has subsided so that one can disconnect the gastrojejunostomy and hook the freed-up segment to the duodenum, to the end of the stomach, after the method of the original Billroth I operation, and in twenty instances Perman has completely relieved this syndrome and it has been equally successful in the two or three instances which we have had with it. Thus these patients are not hopeless.

I recall a seventy-four year old woman who was frail and came to me with a large gastric ulcer four years ago. I thought she probably had a malignancy. We didn't try conservative treatment very long. We found that after two, or three, or four weeks, we could not get her comfortable. Her ulcer was penetrating the pancreas. We could make no reduction in the size of it according to the methods used by our internists, so she was subjected to surgery. She had a benign lesion. She developed the dumping syndrome and at her age it was a difficult problem for her and for everybody. Finally, however, with the help of her physician, she worked out a plan whereby she was able to enjoy life reasonably well, and at the age of seventy-eight she developed a cough, which was quite new. Investigation revealed that she had carcinoma of the lung.

She was then reviewed and I was consulted about it at the time to decide whether I thought it was feasible for a person in her condition to go through or attempt a pneumonectomy. I voted for it. I didn't think she had anything to lose. I thought she had everything to gain. Dr. Richard Sweet took out her lung, with great success, and she is still alive, two years later and probably represents one of the difficult people to kill.

Now, I want to close by mentioning something that Dr. Knies brought out and that is the question of reexamination in these cases. Often enough the first examinations fail to give you what you think the patient may have. I think we must not rely on a negative examination if we feel that the symptoms and physical signs indicate that we are dealing with a lesion. We should not only have gastroscopy following fluoroscopy but these should be repeated, if the symptoms persist, and these ulcers that appear to be healed or nearly healed must be followed because we have had many instances where the inflammatory reaction about an ulcer has subsided during the period of treatment, with the ulcer not quite closed, and then awakened six months later with a hopeless cancer.

I should like to repeat that I would rather have my stomach resected on suspicion and take the chance both of operative mortality and the chance of malfunction afterwards, than to take the certain death that you know has got to come from cancer of the stomach in nearly 80 per cent of the cases.

*Dr. A. X. Rossien (Kew Gardens, N. Y.):*—Since time is of the essence, I should appreciate just a minute or two for discussion.

Permit me to add that I also appreciated the presentations by Dr. Allen and Dr. Rivers. They were most informative and most provocative.

In the study that I have described, the first x-ray recheck was at the end of six weeks and not at the end of two weeks and again at the end of four weeks, as Dr. Weiss described in the method that they used at the Polyclinic Hospital. I was rather interested to know that they did use a routine somewhat similar to the one described by me.

Now to revert back to the study on eighteen cases that I reported last year, when only protein hydrolysate was used. The patients were re-x-rayed at the end of two weeks. One of them had a pyloric and duodenal ulcer which at the end of two weeks revealed no change in either one of the ulcers. One that had only a duodenal ulcer revealed no change. One became inactive. Twelve showed a slight improvement, and one showed no ulcer at the end of the two-week period, which is not as good a record as the combined treatment. It might be added that while I am wholly in accord with Dr. Rivers that practically any type of medical treatment tends to give good results, I believe there are a few advantages here and there in some described medical treatments, and that they are worthy of consideration from that point of view.

At the end of the six weeks, with nothing but protein hydrolysates being used, one of the cases that had pyloric and duodenal ulceration presented no change of the pyloric ulcer, however, the duodenal ulcer became inactive, using the criteria of tenderness and irritability over the duodenal cap as deciding factors as to whether or not it was inactive.

Six other cases became inactive, and at the end of the six weeks period two presented no ulcer, and nine presented improvement.

There is just one little point I want to add, and it is hardly necessary before a body such as this, but recently there seems to have developed the tendency of roentgenologists to report their findings purely on the x-ray picture and not to consider the important role that fluoroscopy plays in deciding whether or not an ulcer is active.

I dare say that purely by the picture one can find that the information thereby gained is misleading. You cannot tell whether an ulcer is irritable and whether or not it is tender unless you see it under the fluoroscope.

*Dr. Philip Thorek (Chicago, Ill.):*—Dr. Morrison discussed the advisability of the transthoracic approach in preference to the transabdominal approach. I most heartily agree with him that the transthoracic approach gives better exposure of the vagi, permits us to get the larger primary vagal trunks, and I dare say results in a more thorovagotomized individual. I may be stepping on some people's toes when I say that the thoracic surgeon has had to learn how to do a good anastomosis now that he does esophageal resections, and the truly abdominal surgeon has had to learn how to resect a rib and mobilize lungs in doing transthoracic vagotomies. The transthoracic approach however does not permit the surgeon to visualize the lesion.

I want to thank Dr. Loder for his very complimentary remarks. He asked "do we have or do I have, failures"? Yes indeed we do have failures. I am ashamed

to say that one of my patients that died—I reported three deaths—died a death of postoperative atony. I couldn't understand why, and I got very shaky on vagotomy and, fortunately, had a postmortem and much to my embarrassment found that I had completely missed the large vagus, the right posterior branch, so that I can't condemn a hemi-vagotomy, if I may use that—vagectomy—Dr. Goldstein, if I may use that term, on the vagotomized individual. This was an old-fashioned, postoperative atony, and had nothing to do with vagotomy whatsoever.

I have had the embarrassing situation of doing a vagotomy in a lady who had an autocholecystojejunostomy misdiagnosed as an ulcer; I saw a crippled duodenum. I had to go back and take down the jejunostomy, and then—and only then—did we get a result.

So we do have failures, but at the end of a year, or some years, as we tally our results, we will find that vagotomy will find a place for itself in the treatment of the gastroduodenal lesions.

Dr. Loder's remark regarding transduodenal severing of the "aneurysm-like thing" was interesting. We are doing more gastrotomies as well as duodenotomies. I realize the gastroscope can tell us something, but when there is the slightest semblance of a doubt, we open the stomach and look at the lesion.

Dr. Loder's idea of going transduodenally might be well taken.

Dr. Goldstein made some very lucid remarks on history. One has to watch his do's and don't's, and dates when talking before such a brilliant medical historian. He mentioned that Dr. Blaine in 1896 discussed vagotomy, however in my article that appeared in the A.M.A. Journal I mentioned Brodie's work, in which he did the first true vagotomy on dogs in 1814, showing there is no response in the production of arsenical gastritis, with arsenic.

Dr. Glass's mucin test is indeed most fascinating, and I dare say might well have a place in the testing of our completeness in vagotomizing individuals. We have been cautious with the insulin test since one or two reports have been published stating that when we give insulin we find some of our patients go into insulin hypoglycemic shock and an occasional case of a coronary thrombosis has been reported.

Dr. Monat mentioned, interestingly enough, five hundred Navy men. Anything can happen to five hundred Navy men! As we all know! However, his statistics are fascinating. Fifty per cent with no acid, 20 per cent low, and 30 per cent high, and Sara Jordan said, "No acid, no ulcer". Which side of the fence are you going to be on?

Wangensteen stated that you can find a case to prove every theory, and you can find that eating gives ulcers and cancers, and starvation gives ulcers and cancers —acid gives it, roughage gives it, eating slowly gives it, eating rapidly gives it. Whichever way we want to go, we will find a theory to help us out.

Dr. Monat's rectal approach to the vagi is brand new, and I dare say will be included in the future approaches that Dr. Goldstein, no doubt, will bring out;

however, the treatment is fascinating. I would do anything to get rid of my ulcer, but I don't think I would let anybody shove a suppository into me and put me to sleep and wake me at three o'clock in the morning to give me a glass of milk. If that will cure it, we will take to that therapy. Our minds are wide open and we will do anything, especially as surgeons, to avoid surgery, but the surgical indications to date are quite clear.

# AN ANION EXCHANGE RESIN FOR THE MEDICAL MANAGEMENT OF PEPTIC ULCER

## (Preliminary Report)

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Clinical experiences with available antacid preparations used in the medical management of peptic ulcers have accentuated the need for a preparation which would not only give symptomatic relief and rapid healing of the ulcer, but also would be devoid of any undesirable side reactions. Most antacids have some effect on the bowel, as for example, aluminum preparations which have a tendency to

TABLE I

| Case No. | Name | Age | Sex | Duration of Symptoms | X-Ray Diagnosis | Length of Treatment | Result |
|---|---|---|---|---|---|---|---|
| 1. | R.A. | 57 | M | 16 yrs. | DU | 8 wks | Excellent |
| 2. | G.F. | 44 | F | 8 " | " | " " | " |
| 3. | S.L. | 37 | M | 3 " | " | " " | " |
| 4. | Wm.F. | 34 | M | 2 " | " | 3 " | " |
| 5. | E.W. | 59 | M | 2 mos. | DU c Obst. | 2 " | Failure |
| 6. | A.K. | 41 | F | 8 " | DU | 4 " | Excellent |
| 7. | I.K. | 40 | M | 5 yrs. | " | 1 wk. | Failure |
| 8. | N.K. | 56 | F | 19 mos. | " | 9 wks. | Excellent |
| 9. | L.M. | 33 | M | 2 yrs. | " | 1 wk. | Failure |
| 10. | F.H. | 54 | M | 18 " | " | 1 day | " |
| 11. | M.A. | 45 | M | 9 " | DU c Obst. | 9 wks. | Excellent |
| 12. | L.H. | 29 | M | 4 yrs. | DU | 4 " | Good |
| 13. | L.L. | 56 | M | 43 yrs. | " | 10 " | Good |
| 14. | M.F. | 47 | M | 24 " | " | 1 wk. | Failure |
| 15. | B.M. | 38 | F | 7 " | " | 7 " | Excellent |
| 16. | L.K. | 26 | M | 5 " | " | 4 " | " |
| 17. | K.K. | 59 | F | 13 " | " | 4 mos. | " |
| 18. | E.O. | 30 | M | 5 " | " | 6 wks. | " |
| 19. | S.S. | 32 | F | 5 yrs. | " | 4 " | " |
| 20. | H.C. | 37 | M | 2 " | " | 6 " | " |
| 21. | S.E. | 35 | F | 4 yrs. | DU | 3 wks. | Excellent |
| 22. | J.P. | 44 | F | 4 " | " | 2½ wks. | " |
| 23. | J.R. | 56 | M | 31 " | None | 6 wks. | " |
| 24. | T.G. | 47 | M | 21 " | DU | 9 " | " |
| 25. | M.H. | 53 | M | 14 " | " | 6 mos. | " |
| 26. | S.S. | 58 | M | 1 yr. | " | 2 wks. | " |
| 27. | H.O. | 34 | M | 3 yrs. | " | 3 " | " |
| 28. | A.W. | 35 | M | 1 yr. | Neg. | 3 " | " |
| 29. | G.S. | 39 | M | 6 mos. | DU | 3 mos. | " |
| 30. | P.O. | 64 | M | 4 " | " | 1 mo. | " |

constipate; others produce diarrhea, and there are those whose use causes acid rebound, or affect the acid-base equilibrium and produce alkalosis.

A new therapeutic agent, a synthetic resin, a polyethylene polyamine methylene substituted resin of diphenylol dimethyl methane and formaldehyde in basic form, was introduced by Spears and Pfeiffer[1] and Kraemer[2-4] for the medical

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management of peptic ulcers. This substance, an anion exchange resin, produced prompt symptomatic relief and eventual cures in a fairly large percentage of patients.

According to these investigators, this anion exchange resin had no effect on bowel function, did not affect the acid-base balance of the blood, produced no acid rebound and did not disturb the electrolytes. The anion exhange resin thus gave the indication of being a substance possessing many if not all the virtues of an ideal antacid.

Prior to the clinical application of this resin, Segal and associates[5] reported that it was non-toxic in laboratory animals even when fed in large amounts, over a long period of time. They also demonstrated that the resin effectively reduced the acidity of hydrochloric acid solutions and of gastric juice. These findings were confirmed by Martin and Wilkinson[6] who found that the resin also inhibited pepsin activity and that the particle size of the resin was a major factor in its adsorptive capacity.

TABLE II

Result of Resin therapy in 30 Cases of peptic ulcer

| Result | Cases | Per cent |
|---|---|---|
| Excellent | 23 | 76.6 |
| Good | 2 | 6.6 |
| Failure | 5 | 16.6 |

## Clinical Material

In attempting to further evaluate its usefulness in the symptomatic therapy of peptic ulcer, the anion exchange resin (now known as Resinat), was used in a series of twenty-seven private and three clinic cases. These patients were unselected and taken seriatum. All had typical ulcer histories, and all but two had positive roentgen findings. Of these two non-x-rayed cases, one (Case 23) was included because of overwhelming clinical evidence of ulcer (30 years of recurrent ulcer pain, two bouts of melena; and operation in 1922 for a perforation). The second (Case 28), with a typical year's history, was not x-rayed until after Resinat had been given for fifteen days, at which time no lesion could be demonstrated. Most of them previously had various types of orthodox antacids without relief. A brief summary of these cases appears in Table I.

## Method

The anion exchange resin (200 Mesh) was available in two forms: capsules containing 0.25 gram each and cachets of one gram. These were used interchangeably, the usual dose being 2-4 capsules or one cachet every two hours during waking time, with additional doses if required for night pain. A generous bland

diet was allowed and the use of other medication (sedatives, antispasmodics) restricted as much as possible. All the patients were ambulant. As symptoms subsided the dose was given every three hours and maintained from four to six weeks and longer when possible.

## Results

Complete freedom from symptoms within five days after commencing the resin therapy was designated an excellent result. Patients requiring more than five days for complete relief, or those reporting only partial relief, are classified as good, while those securing little or no relief are listed as failures in this report. These findings are indicated in Table I and summarized in Table II.

From this it is apparent that five-sixths (83.2 per cent) of cases treated were favorably influenced by resin either to the point of complete relief of symptoms, or (in the "good" cases), to a degree greater than that obtained with previously used alkalis. It is to be noted that one of the unrelieved cases took the resin only one day, and that two others discontinued it after one week. It is entirely possible that more continued use might have resulted in a more favorable outcome.

No side effects of any kind were reported by the patients or noted during this study.

During the follow-up period, which is now fourteen months, for the earliest case, two recurrences have taken place. One (Case 15) recurred three months after discontinuing the resin; the other (Case 8) after one week's omission of the drug.

## Summary and Conclusions

1. An unselected group of thirty duodenal ulcers were treated with an anion exchange resin.

2. Twenty-three (76.6 per cent) were completely free of symptoms in five days or less; two (6.6 per cent) were relieved to a greater degree than with previous alkali therapy.

3. No side effects (on bowel function, gastric secretion, or acid-base balance) were clinically demonstrable.

4. It is therefore concluded that an anion exchange resin of this type is a useful adjunct in the symptomatic treatment of peptic ulcer.

The Author expresses his thanks to Steven Horoschak for his cooperation in this study and to the Medical Research Department of the National Drug Company of Philadelphia, Pa., for the supply of Anion Exchange Resin which is now available under the name of Resinat.

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# EDITORIAL

## The Development of Vagotomy in the Treatment of Gastric, Duodenal, and Jejunal (Anastomotic) Ulcer

Ulcer of the stomach, duodenum, and anastomotic or marginal ulcer have been subjects for discussion for many years. Gastroduodenal ulceration affects a great many persons of civilized countries, of high and low station, old and young. Thus, one may here recall the ulcer cases of Aristotle, Tatian (perhaps, Marcus Aurelius also had an ulcer, since Galen treated him for gastric disturbances) Cardinal Caesar Baronius, of Sorano, Henrietta-Anne, of England; Jean D'Arcet, Napoleon Bonaparte, and probably Catherine of Braganza. T. Bonet, of Geneva, cites John Bauhin's case of a perforated ulcer in a physician's young wife. Charles Darwin, Herbert Spencer, Thomas Henry Huxley, Thomas Carlyle, Harry Hopkins, Rudolf Valentino, Clark Clifford, James Roosevelt, and others suffered from ulcer.

Pericles, Athenian Statesman, who died in the autumn of 429 B.C., probably suffered aggravation of his ulcer and abdominal pains by the threatened hostilities between Athens and Sparta (431 B.C.) and the worries caused by his many adversaries, their threats to his friends and their many scandalous charges against him and his friends. The death from the plague, of his two sons and sister also may have contributed to this.

Dr. Peter Middleton, who was a member of the first medical faculty of King's College, now Columbia University, died in New York in 1781. He suffered from gastric ulcer and malignancy. John Wakefield Francis reported the presence of a tumor obstructing the pylorus.

I also cite here the reports by Panthot of Vice-Dean de Rhode's case; Morgagni's report of Tyson's case; the interesting report by Cruveilheir, of the case of Jean D'Arcet, French chemist and physicist in "Pathological Anatomy of the Human Body". The report by J. Schenck, and Dodonaeus a woman of 60 years; Donatus' case of Camillus Facinus, 59 years old, in "De Medica Historia Mirabili", Mantua, 1586; Bartholin and Borrichius's report; Alex Littré's report of a 16 year-old-youth with perforated ulcer, and the cases of Christopher Rawlinson, and Jacopo Renada of Padua-Domenico Miazzo, who died of a perforated duodenal ulcer on June 23, 1791.

Several informative reviews and reports on the subject of vagotomy have appeared in recent literature including articles by Alvarez; McCrea; Hartzell; Pierre Wertheimer, Peter (Gertsen) Herzen, of Moscow, A. M. Cheshkoff, J. A. Schilling et al., I. F. Stein et al., of Chicago, and Ralph Colp, of New York City. Since January 1943, when Dragstedt, of Chicago reintroduced and revived vagotomy (transthoracic and transabdominal) for the treatment of intractable and/or recurrent ulcer many reports of successes and some failures, too, have appeared in literature. It seems, that at present, just six years after the "rebirth" of vagotomy, much of the earlier enthusiam has disappeared. Now, this procedure is

being limited to cases of marginal or anastomotic ulcer. Even in some cases of gastrojejunal ulcer, surgeons have recently had a number of failures and have now become reluctant to advise vagotomy for marginal ulcer! Thus, Colp of Mount Sinai Hospital, New York, is definitely of the opinion, that vagotomy with its many drawbacks and failures, will be relegated to a much less prominent place for the surgical treatment of ulcer! It should be recalled here, that Colp has performed bilateral vagotomy since 1938 and 1939 and has tried both the transthoracic and transabdominal routes, with and without subtotal gastrectomy. He is emphatically opposed to the free and overenthusiastic use of this procedure in the treatment for ulcer of the stomach, duodenum and jejunum! *Vagotomy as a sole procedure is definitely being abandoned.* Some of the early experimental and clinical work might briefly be reviewed at this time.

Sir Benjamin Collins Brodie (1814) observed the prompt reduction in acid gastric secretion following vagotomy in dogs. Brodie made his report on "Experiments and observations on the Influence of the Nerves of the Eighth pair on the Secretions of the Stomach" before the Royal Society (London) in 1814. Brodie, it may be recalled, was Sir Everard Home's pupil. Wassman (1839) discovered pepsin, and Wm. H. Prout (1824) discovered hydrochloric acid in the gastric juice and what problems have arisen from these discoveries! We are not much further advanced in 1949 than were the earlier workers in this field decades ago. We are still in the experimental and "try everything" stage, insofar as successful control of the ulcer is concerned. The many forms of medical therapy with the multiplicity of remedies, of all kinds of antacids, adsorbents, hormones, sedatives, and antispasmodics, and the various recommendations of this or that method of surgical procedure, give ample evidence that we have not yet available a universally successful and acceptable form of treatment for gastroduodenal ulcer, either medical or surgical, that will insure our patients against recurrences and complications, and annoying and distressing sequelae! Karl A. Meyer, Rosi and Stein, of Chicago state "It is still too early to make a final evaluation of vagotomy in the treatment of peptic ulcer". "Until more information is available concerning the possible late sequelae, the use of vagotomy should be limited to clinical investigation with one exception". "*Complete* vagotomy is a method of choice in the treatment of marginal ulcer following gastric resection". Colp does not believe *truly complete vagotomy*, i.e., cutting all the vagus nerves and smallest fibres, is possible, and he has tried to do it by using both the transthoracic and transabdominal routes! The publications of Usher Parsons (1840), Pavlov (1894), Jakob Kaufmann (New York), Franz Alexander (Chicago), Dragstedt, and others have shown that the cephalic or neurogenic phase of hyperacidity and ulcer recurrence is no longer a figment of the imagination! However, the "ulcer diathesis"—the ulcer problem, still remains unsolved!

Pavlov found in dogs, that hydrochloric acid was never present following section of the vagus nerves. He confirmed these observations for six months (1895-1896).

While they did not resort to vagotomy to control hyperchlorhydria and resulting gastric disease, Michael Ettmüller and Sir Gilbert Blane observed cases of hyperchlorhydria or "hyperacidity" with inflammation of the stomach and knew of the need for using alkalis to neutralize acidity.

Ettmüller, in his "Practice" (1685), discusses inflammation of the stomach and the need of alkalis for the acidity. Blane, in presenting his report on 1 March 1796, discussed the functions of the stomach, stating: "this is no new remark of mine, but I can testify the truth of it from my own experience." Then, in Observation II, he states, "The next complaints I have to mention, in which I have observed these remedies [alkalis] to be useful, are certain cases of indigestion, especially those in which *acidity is the prevailing symptom* (italics ours). In these I have had the most unequivocal proofs of the good effects of lime water and *pure alkalis . . .*"

"In reasoning upon these facts the most obvious idea that presents itself is, that *these medicines act by destroying the acidity* (italics ours)—the mild alkalis, magnesia and the common calcareous earth ought to have much greater power, (of absorbing acid) as they can be taken in much greater quantities. This is not the case. But, in chronic diseases of the stomach in adults, these have merely a paliative (neutralizing) effect, while the pure alkalis and lime water have an evident effect in correcting the function of the stomach itself and thereby producing permanent relief. These medicines and—it is conceivable and even highly probable that they may act on what may be called *the gastric acid, which may be secreted in so concentrated a state as to constitute disease. I have satisfied myself that there is such an acid,* (italics ours) by applying the usual tests to the inner surface of the stomach of animals." This antacid form of therapy was definitely carried out by G. Blane 153 years ago.

P. Herzen, of Moscow, published his interesting observations "Les causes de mort après la double vagotomie dans leur rapport avec les conditions de survie" (Lausanne, L. Vincent, 1897). Cheshkoff, in 1902, observed a dog for a year and seven months after simultaneous excision of both vagus nerves in the neck (St. Petersburg, P. P. Soikin, 1902). H. C. Wood, Jr. (1870) reported the results of his experimental vagotomy on dogs, before the Philadelphia College of Physicians including the effect of vagotomy on intestinal motility.

Among the many contributions to this subject may be mentioned the work of A. Latarjet, and Pierre Wertheimer, of Lyon, France; A. J. Carlson, Charles H. Mayo, Leubuscher and Schäfer, E. Bircher, Winkelstein and Berg; Pieri and Tanferna, of Italy, who performed transthoracic and transabdominal bilateral vagotomy for ulcer; Alvarez, of Mayo Clinic, Schiassi; Schiff; Stierlin; Borchers; Foa; Dudek, and more recently, Lester R. Dragstedt of Chicago, Walter Lincoln Palmer, K. S. Grimson, Waltman Walters, Francis D. Moore, I. S. Ravdin, Duncan A. Cameron, Ralph Colp, Samuel F. Marshall, and many others have contributed to the rapidly accumulating literature on the subject!

Ernst Unger, Bettmann and Rubaschow wrote on "Bilateral Vagotomy", thirty-eight years ago (1911), as did also, K. Fritsch (1910-1911). Adolf Widmer (1893) studied the effects of unilateral vagotomy and resection of the vagus in humans fifty-six years ago. S. Rubaschow in 1912, reported on the effects of vagotomy, as did also Max Littauer in 1920. It is interesting to note, too, that J. M. Lasowsky and A. N. Ptschelina contributed a report on bilateral vagotomy. Finally, the papers by A. Frouin and E. Pozenski, Gianolla, D. Giordano and Einar Thomsen have been generally overlooked by Dragstedt, Grimson, Griswold, Colp, Waltman Walters and others.

It should be recalled, in closing, that several decades ago, a number of men, performed vagus section for the relief of pain in cases of tabetic gastric crises. Perhaps, many of their (luetic) ulcer patients were thus also relieved of their ulcer complaints!

HYMAN I. GOLDSTEIN

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## CHAPTER ACTIVITIES

### New Jersey Chapter

The annual open meeting of the New Jersey Chapter was held at the Academy of Medicine in Newark, on 1 December 1948.

Preceding the meeting a dinner was tendered Dr. Z. T. Bercovitz, the guest speaker.

At the scientific session which followed, Dr. Bercovitz spoke on "Diagnosis and Treatment of the Diarrheas".

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### New York Chapter

The next regularly scheduled meeting of the New York Chapter will be held at the New York Academy of Medicine on 10 January 1949.

The scientific portion of the program will consist of "Surgical Approach in Cases of Postcholecystectomy Syndrome" by Dr. Franklin R. Carter, Attending Surgeon, Post Graduate Hospital and "Roentgenological Studies of the Small Intestines in Children" by Dr. John H. Dale, Jr., Associate Professor of Pediatric Roentgenology, Cornell University.

Members of the medical profession and their friends are cordially invited to attend.

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## NEWS NOTES

### More Speakers Accept Convention Invitations

Following the announcement in last month's issue that Dr. Frank H. Lahey would speak at the Fourteenth Annual Convention of the National Gastroenterological Association, Dr. William Reid Morrison, President and Chairman of the Program Committee has received several more acceptances.

Drs. C. Stuart Welch, Boston, Mass.; John M. T. Finney, Jr., Baltimore, Md. and William B. Castle, Boston, Mass. will participate in the Convention program as guest speakers.

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### Executive Board Meeting

A meeting of the Executive Board of the National Gastroenterological Association was held in New York City on 6 December 1948.

Routine correspondence was properly disposed of.

The Association was advised of the death of Drs. E. Roland Snader, Jr., Philadelphia, Pa.; Victor M. Gore, Tucson, Arizona and Charles V. Crane, Grand Rapids, Michigan. The Secretary was instructed to send letters of condolence to the families of the deceased.

Dr. Roy Upham, Secretary-General reported that the New York and New Jersey Chapters had held meetings and that the next scheduled meeting of the New York Chapter would be held on Monday evening 10 January 1949.

Upon presentation of the necessary qualifications Dr. Donald C. Collins, Hollywood, Calif.; Dr. Daniel Diamond, Brooklyn, N. Y. and Dr. Hyman Fisher, Sunmount, N. Y. were advanced to Fellowship. Dr. Leon Littman, Brooklyn, N. Y. was advanced to Associate Fellowship.

The Boston, Louisiana, Memphis, New Jersey, New York and Philadelphia Chapters presented for ratification the applications of the following which applications were accepted as follows: Dr. Howard A. Bouvé, Boston, Mass., Associate Fellow; Dr. Alexander J. A. Campbell, Boston, Mass., Fellow; Dr. John H. Crandon, Boston, Mass., Fellow; Dr. Joseph Duggan, Malden, Mass., Fellow; Dr. Dwight E. Harken, Boston, Mass., Fellow; Dr. Francis T. Jantzen, Boston, Mass., Associate Fellow; Dr. John H. McGowan, Quincy, Mass., Member; Dr. Louis H. Nason, Boston, Mass., Fellow; Dr. Max Ritvo, Boston, Mass., Fellow; Dr. Joseph Tartakoff, Boston, Mass., Fellow; Dr. Carl H. Rabin, New Orleans, La., Fellow; Dr. R. L. Sanders, Memphis, Tenn., Fellow; Dr. Emil L. Santangelo, Paterson, N. J., Member; Dr. Ludwig Simon, Newark, N. J., Member; Dr. J. Edward Astrachan, Bellaire, L. I., Member; Dr. Samuel S. Feuerstein, Long Island City, N. Y., Member; Dr. Maurice E. Kleinberg, Brooklyn, N. Y., Member and Dr. Hans A. Sylvester, Philadelphia, Pa., Member.

Drs. Raymond Harry Hirsch, Nashville, Tenn.; Omer Rumbos, Caracas, Venezuela; Winston A. Sargent, Brattleboro, Vt.; Carlos Suarez, El Tocuyo, Lard, Venezuela; Harry Menton, Moline, Ill.; and Vikit Viranuvatti, Bangkok, Siam were elected to membership at large.

Reports of the various committees were presented and accepted.

The resignation of Dr. Frank C. Yeomans, for many years a member of the National Council, the Executive Board, and chairman of the Memberhip Committee, because of inability to actively participate in the affairs of the Association, was accepted with regret.

The Secretary was instructed to thank Dr. Yeomans for his untiring efforts on behalf of the Association.

The Secretary then advised the Board that a vacancy existed in the membership of the Board.

Under the provisions of the Constitution, the Board proceeded to elect Dr. Horace W. Soper, St. Louis, Mo. to fill Dr. Yeomans' unexpired term.

Dr. Morrison appointed Dr. William C. Jacobson as chairman of the Membership Committee to succeed Dr. Yeomans.

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### Third Interamerican Congress of Radiology

The Third Interamerican Congress of Radiology will be held in Santiago, Chile, 11-17 November 1949.

Dr. James T. Case has been named as coordinator between the Executive Committee and the United States Radiologists.

The official scientific subjects of the Congress will be: 1) Radiological exploration of the cardiovascular system with opaque material; 2) Diagnosis and simple radiological exploration of the skull; 3) Radiation treatment of cancer of the tongue; 4) Radiation treatment of cancer of the cervix.

Further details concerning the Congress may be obtained from: Comite Ejecutivo Del III Congreso Inter-Americano de Radiologia, Casilla 693, Santiago de Chile.

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### Mississippi Valley Medical Society 1949 Essay Contest

The ninth Annual Essay Contest of the Mississippi Valley Medical Society will be held in 1949. The Society will offer a cash prize of $100.00, a gold medal, and a certificate of award for the best unpublished essay on any subject of general medical interest (including medical economics and education) and practical value to the general practitioner of medicine. Certificates of merit may also be granted to the physicians whose essays are rated second and third best. Contestants must be members of the American Medical Association who are residents and citizens of the United States. The winner will be invited to present his contribution before the Fourteenth Annual Meeting of the Mississippi Valley Medical Society to be held in St. Louis, Mo., Sept. 28, 29, 30, 1949, the Society reserving the exclusive right to first publish the essay in its official publication the *Mississippi Valley Medical Journal* (incorporating *Radiologic Review*). All contributions shall be typewritten in English in manuscript form, submitted in five copies, not to exceed 5,000 words, and must be received not later than May 1, 1949. The winning essays in the 1948 contest appear in the January 1949 issue of the *Mississippi Valley Medical Journal* (Quincy, Illinois).

Further details may be secured from: Harold Swanberg, M.D., Secretary, Mississippi Valley Medical Society, 209-224 W.C.U. Building, Quincy, Illinois.

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Dr. George T. Pack, Member of the Editorial Council of The Review of Gastroenterology has recently been elected Honorary Member of the Brazilian Proctologic Society.

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# ABSTRACTS

## Esophagus

THE ANATOMY OF THE PERIESOPHAGEAL VAGI. H. Doubilet, Shafiroff and Mulholland. Ann. Surg. **127**:128-135, (Jan.), 1948.

Since vagotomy or vagus nerve resection for peptic ulcer has become a frequently used surgical procedure—it is timely for these authors to re-investigate the anatomy of the esophageal vagi. A total of 32 gross dissections on cadavers were carried out and the esophagus and its associated nerve structures were carefully examined.

The total number of vagal fibres passing through the esophageal hiatus were not limited, as commonly conceived, to an anterior and posterior branch, but frequently came through as three or four branches. The hepatic nerve or nerves were traced through the layers of the lesser omentum to the liver.

Surgical denervation can be accomplished by means of periesophageal stripping, through the left chest exposure of the infra-aortic esophagus. Hyman I. Goldstein

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CARCINOMA OF THE ESOPHAGUS. Michael E. Debakey and Alton Ochsner. Postgrad. Med. **3**:192-198, (Mar.), 1948.

Carcinoma of the esophagus has become increasingly important because of its relative frequency and the progress recently made in surgical treatment. The disease occurs predominantly in elderly male individuals, and is most commonly found in the lower two-thirds of the esophagus. Histologically it appears as the more common squamous cell variety, and the adenocarcinoma, which is most frequently seen in the lower portions of the esophagus.

The earlier stages of the disease are insidious, vague and intermittent. A sense of oppression or fullness in the chest, heartburn, epigastric distress are complaints which lead several months later to a definite dysphagia. Regurgitation may follow together with the typical symptoms of anorexia, loss of weight and increasing weakness. The average duration of symptoms before a diagnosis is made is frequently four to six months. The diagnosis is established by esophagoscopy, x-ray and fluoroscopy. The only cure consists in the removal of the tumor bearing area together with regional lymph nodes, and a restoration of the continuity of the alimentary tract by intrathoracic esophagogastrostomy. The results of surgery of the esophagus in recent years has shown gratifying progress. The immediate mortality in the hands of the authors has decreased from 75 per cent to 25 per cent, and five year cures have given rise to an 11 per cent survival rate. Jacob A. Riese

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## Gastrointestinal Tract

KAPOSI'S DISEASE. REPORT OF A CASE WITH UNUSUAL VISCERAL MANIFESTATIONS. Kenneth H. Seagrave. Radiology. **51**:248, (Aug.), 1948.

Kaposi's disease is an uncommon but interesting type of tumor, of low-grade malignancy, which may involve any part of the body. The growth is also called, more properly, multiple idiopathic hemorrhagic (pigmented) sarcoma. The cutaneous manifestations characteristically appear on the extremities as elevated vascular nodules which become pigmented. Visceral involvement is less frequent. In the described case, the initial growth was in the nasopharynx, followed by characteristic skin lesions and later by evidence of devastating gastrointestinal involvement. The roentgenological examination revealed intraluminal masses throughout the small intestine which proved to be polypoid growths of multiple hemorrhagic sarcoma. Franz J. Lust

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MESENTERIC VASCULAR OCCLUSION. J. D. Rives, Strug and Essrig. Ann. Surg. **127**:887-905, (May), 1948.

Obstruction of mesenteric blood vessels by thrombosis or embolism, if we include minor accidents that occur in gangrenous appendicitis, peritonitis, strangulated hernia, operative trauma, etc., is a very common condition. The authors discuss mesenteric vascular thrombosis or embolism resulting from other causes than local infection or injury. They report on 19 cases found in the records of Touro Infirmary 1938-1947. Eleven cases of this series were seen by the authors during the past two years.

Nominal branches of the mesenteric arteries are "functional end arteries", although they communicate with each other freely through a profuse submucous plexus. The authors discuss the prognosis, treatment, the clinical picture, diagnosis and operative findings. They include a bibliography of 58 references to the literature. Hyman I. Goldstein

## Pathology and Laboratory Research

THE ACTION OF GASTRIC CONTENTS ON TUBERCLE BACILLI. V. M. Schwarting. Am. Rev. Tuberc. **58**:123-128, (July), 1948.

Three-fourths of adult gastric lavages are harmful to tubercle bacilli. Delay permits inhibitory lavages to kill off many of the bacilli thus producing false negative cultures.

In a series of 50 seeded gastric lavages, 38 or 76 per cent, were bactericidal for tubercle bacilli. Inhibitory lavages were acid and usually contained some pepsin. Natural gastric lavages, which may contain bile, saliva, cellular elements and germicidal factors, are more strongly inhibitory than artificial gastric juices. The bactericidal effect of gastric lavages is directly related to the length of time and the height of temperature at which lavages are kept.

The best results (cultural) are obtained if lavage specimens are digested and cultured as soon after collection as possible.

Hyman I. Goldstein

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## Pancreas

FIBROCYSTIC DISEASE OF THE PANCREAS. Lowell S. Goin. Radiology. **51**:36, (July), 1948.

Fibrocystic pancreatic disease is a congenital, familial, highly fatal disease of infants, regularly accompanied by pulmonary changes which are demonstrable in the roentgenogram. The disease has become recognized as a clinical entity only in the past ten years due almost entirely to the work of Dorothy Andersen. The cause of the disease remains unknown. The histopathologic factor is that of obstruction of the smaller pancreatic ducts and subsequent dilatation of the acini. There is a severe Vitamin A deficiency. The lung changes are the basis of the roentgenological findings. There are bilateral hilar densities, with mottled linear densities extending outward, marking a sort of aura about the cardio-vascular shadow. Bronchopneumonic patches are seen, and a honeycomb appearance of the lung bases frequently represents bronchiectasis. The bronchopneumonic areas may be quite extensive, and bronchopneumonia is commonly the immediate cause of death. The symptoms and clinical findings are those of gross deficiency of pancreatic secretion. The stools are bulky, foul and gray, the abdomen is distended. The fat contents of the stools is 60 per cent, there is a delayed glucose absorption and a poor Vitamin A absorption. Diarrhea and repeated respiratory infections develop. Vitamin A up to 150,000 units per week and casein hydrolysates should be given instead of milk.

Franz J. Lust

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ACUTE PANCREATITIS (80 CASES). J. M. Howard and I. S. Ravdin. Am. Practitioner. **2**:385-395, (Feb.), 1948.

Diagnosis of acute pancreatitis is now made more accurately and more frequently than ever before. Practical enzyme determination and improved diagnostic ability on the part of the clinician, explain the more frequently-made correct diagnosis of "acute pancreatitis". The authors have studied the cases of the past 25 years—1922 to 1946. Only cases of "idiopathic" acute pancreatitis are included—not "secondary" cases—i.e., posttraumatic or following perforation (ulcer, etc.).

Every case in this series has been proven by exploratory laparotomy, serum enzyme determination (amylase and lipase) and calcium drop in concentration; or, by necropsy. A temporary decrease of insulin occurs, but without hypoglycemic shock. There is then a rise in the blood sugar, with pancreatic inflammation. None of the patients were previously diabetic. There was evidence of bacterial infection in 19 of 34 patients in whom bacteriologic studies were made. In the edematous type of cases pure cultures of staphylococci were found in over 50 per cent of the cultures taken—this infection may be a secondary bacterial invasion. Acute cholecystitis was present in 22 patients. Thirty-one patients were jaundiced.

Surgical decompression of the biliary tract has been done frequently, because of the high incidence of biliary tract complications. Penicillin, streptomycin and sulfonamides are used as soon as the diagnosis has been made. Intubation of the stomach or small bowel are helpful. The administration of fluids parenterally are necessary—and helpful. Insulin is occasionally needed. The authors followed-up 47 patients, subsequent to the disease from one to 24 years. Mild diabetes developed in several instances, but no evidence of pancreatic calculi, calcification, or cyst.

Hyman I. Goldstein

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DIFFUSE PANCREATIC CALCIFICATION. Robert J. Reeves and Frank T. Moran. Radiology. **51**:219, (Aug.), 1948.

The authors describe the case of a four year old child with diffuse pancreatic calcification, apparently the earliest case on record. Besides, five other cases, all under 35 years of age are reported. All of them had severe complaints for two to eight years. The child never had abdominal pains. Two patients gave a history of excessive alcohol consumption. Four cases had diabetes mellitus. Serum amylase was increased in one case. The roentgenologic finding of calcium within the pancreatic

parenchyma is of considerable significance. Since it becomes deposited in areas of fat necrosis, fibrosis, or degenerative tissue it indicates the site of a pathologic process. Two cases had pancreatic achylia. Due to the pains, one case bordered on drug addiction, another had such intractable pains, that bilateral ganglionectomy had to be performed. FRANZ J. LUST

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CHRONIC RECURRENT PANCREATITIS (20 CASES). S. N. Maimon, J. B. Kirsner and W. L. Palmer. Arch. Int. Med. **81**:56-72, (Jan.), 1948.

Chronic pancreatitis is characterized by recurrent episodes of pain in the upper abdomen. Clinical diagnosis is seldom made. There were 12 men and 8 women in these cases. This entity appears to be more common in men than women, with the incidence greater in patients under 50. Vague digestive disturbances and transitory abdominal discomfort were present almost constantly. Pain was the chief symptom; bloating and eructation were quite frequent. Chronic alcoholism may be a contributing factor. Loss of weight occurred in 12 patients of this series.

Recurrent jaundice with attacks of pain occurred in 8 cases. Serum amylase was increased in 3 cases of 8 patients studied. A diabetic type of curve was observed in 8 of the cases—with the oral glucose tolerance test. Icterus index was increased in 7 of 9 cases studied. Bilirubinuria was present in six patients. The leucocyte count was increased in 12 patients. Steatorrhea was present in 5 cases. Calcifications (pancreatic) were demonstrated in 4 of these. All five were diabetic. Sixteen of the 20 patients were surgically explored. Drainage of the common duct or gallbladder was performed in 6.

Roentgenograms of the upper gastrointestinal tract may demonstrate constriction of the duodenum by fibrosing pancreatic lesions and displacement of the lesser curvature by a pancreatic cyst, and pancreatic calculi may be demonstrated. Disturbances of carbohydrate metabolism are frequent.
HYMAN I. GOLDSTEIN

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## BOOK REVIEWS

LECTURES ON THE LIVER AND ITS DISEASES: H. P. Himsworth, M.D., Professor of Medicine in the University of London, Fellow of the Royal College of Physicians of London. 204 pages. Harvard University Press, Cambridge, Mass., 1947. Price $5.00.

This monograph is based on a series of lectures delivered at the Lowell Institute, Boston, in March 1947 by Professor Himsworth, Director of the Medical Unit, University College Hospital, London.

The author, in twelve chapters, discusses the types of liver injury and their structural consequences, the vascular factor in liver injury, nutritional factors in liver injury, experimental and human, noxious factors causing liver injury, the syndromes of hepatic cirrhosis, enlargement of the liver, portal obstruction, liver function tests, and puncture biopsy of the liver are discussed briefly in Chapter VI. In the next chapter the author presents "The Clinical Classification of Liver Disease" in one and one-half pages!

Infiltrations of the liver and postinfiltrative fibrosis, parenchymatous hepatitis, chronic massive hepatitis, and clinical sequences in parenchymatous hepatitis are very briefly touched upon.

In the closing chapters (X, XI, and XII), Professor Himsworth discusses cholangiohepatitis, obstruction to the bile ducts and biliary diffuse hepatic cirrhosis brief mention being made of Hanot's "hypertrophic biliary cirrhosis" and Schottmuler's (1921) "cholangitis lenta". Thrombosis of the portal vein, hepatic artery occlusion and occlusion of the hepatic veins (acute and chronic obliterating endophlebitis) focal lesions of the liver, and hepatic lesions in thyrotoxicosis, and cancer of the liver (primary and secondary) are briefly cited. This book is of interest to clinicians, gastroenterologists, and general practitioners of medicine.

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THE ENGAGED COUPLE HAS A RIGHT TO KNOW, A MODERN GUIDE TO HAPPY MARRIAGE. Abner I. Weissman, M.D., foreword by Abraham Stone, M.D. 256 pages. Renbayle House, New York, N. Y., 1948. Price $3.00.

Dr. Weissman although not a psychiatrist, hit the keynote for engaged couples. He discusses, and frankly so, the role of sex. He goes into the matter of blood incompatibility and sterility. He touches on marriage and the honeymoon.

It is recommended by the reviewer that this book be on the shelf of every physician regardless of what he specializes in.

ARTERIAL HYPERTENSION. David Ayman, M.D., Instructor in Medicine, Tufts College Medical School; Associate Visiting Physician Beth-Israel Hospital, Boston, Mass. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D., M.A.C.P., Boston. 92 pages. Oxford University Press, New York, 1948. Price $2.50.

This excellent little monograph reprinted and revised from Oxford Loose-Leaf Medicine, written by an expert on hypertensive cardiovascular diseases and edited by an able clinician, will be a welcome addition to every physician's library, especially to those physicians interested in hypertension.

Among topics briefly discussed are pathology, symptomatology, evolution of essential hypertension, diagnosis, and 37 pages on "Treatment".

The rice diet (Kempner, 1945; 1946) receives only brief mention (page 257) in a single paragraph. Weight reduction, psychotherapy, and sympathectomy, receive only brief consideration. This little volume may be quite helpful to students and internes and resident physicians.

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DISEASES OF THE WARM CLIMATES: THEIR FEATURES, DIAGNOSIS AND TREATMENT. Albert Dubois, M.D. and Louis Van Den Berghe, M.D., Sc.D. 445 pages. Grune & Stratton, New York, 1948. Price $10.00.

Doctor Dubois, Director of the Institute of Tropical Medicine (Antwerp), and Doctor Van Den Berghe, Professor of the Institute of Tropical Medicine, are fully qualified for the successful task of publishing a practical and very informative volume on "diseases of the warm climates".

They have had long experiences in tropical medicine in the Belgian Congo and in other parts of the world. Dr. Dubois is an expert leprologist. Both authors have studied tropical diseases in Africa, Asia (including India) and other parts of the world. Consideration is given to the geographical distribution of the socalled 'Tropical Diseases', Cosmopolitan Diseases in the Tropics, African Trypanosomiasis, Chagas' Disease (American Trypanosomiasis), Malaria, Relapsing fever, Rickettsial Diseases, (including Rocky Mountain Spotted Fever), Bartonellosis (Oroya fever), Plague and Dengue.

The various "Intestinal Diseases" are ably and instructively discussed in Chapter V, in sixty-six pages of text. Bacillary Disentery, Amebiasis, Cholera, Ancylostomiasis and, Schistosomiasis are concisely and acceptably presented. Skin diseases are covered in 87 pages of text (Chapter VI). Leprosy, coccidoidomycosis, histoplasmosis, yaws, leishmaniasis, granuloma venereum, filariasis and elephantiasis are given brief consideration.

Avitaminosis (deficiency diseases), while not peculiar to the tropics, also are discussed by the authors, in Chapter VIII. Of interest, and of considerable value, are the appendices A, B, and C. Here, specialized drugs and their dosage are considered. Simple laboratory procedures aiding in the diagnosis of diseases of warm climates are described in Appendix C.

This timely volume, in this speedy airplane-era, making the world much smaller "in time and travel", is highly recommended for all physicians interested in tropical diseases.

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CANCER, DIAGNOSIS, TREATMENT AND PROGNOSIS. Lauren V. Ackerman, M.D., Assistant Professor of Pathology, Washington Univ. School of Med., Pathologist to the Ellis Fischel State Cancer Hosp. and Juan A. del Regato, M.D., Radiotherapist to the Ellis Fischel State Cancer Hosp., Formerly Assist. to the Radium Institute of the Univ. of Paris. 745 text illustrations and 42 color reproductions. 1115 pages. C. V. Mosby Co., St. Louis, 1947. Price $20.00.

The authors modestly state that "this book is not an encyclopedic dissertation of all knowledge of cancer". This book does contain much of value, contributes to our general knowledge, and facilitates our understanding of many problems connected with cancer. The clinician, the surgeon, the student, the general practitioner, and specialists in other branches of medicine and surgery, will profit by reading this excellent book on Cancer.

Dr. Eugene Bricker, Associate Professor of Surgery at Washington Univ. School of Med. edited the (Chapter V) section on "Surgery of Cancer" (pages 88-94). The chapter on "Cancer Research" (pages 30-59) is contributed by Dr. Michael B. Shimkin, of the National Cancer Institute. The authors are to be highly commended for the excellence of the illustrations included in this one volume "magnus opus"—particularly for the fine colored plates. The publishers are to be congratulated for the fine paper, and the manner in which the illustrations were reproduced. The reviewer considers this the best one volume textbook on "Cancer". This volume is the culmination of many years of experience and hard work, and close application to this all important subject—"Cancer, Diagnosis, Treatment and Prognosis". "Pathology of Cancer and Radiotherapy of Cancer" receive adequate consideration for the benefit of most of the readers of this work.

Among the many subjects discussed are Cancer of the Skin, of the Respiratory System and Upper Digestive Tract, Tumors of Mediastinum, Cancer of the Digestive Tract (Chapter X, 201 pages), Cancer of the Genitourinary Tract and, of the male and female genital organs, Cancer of

the Mammary Gland, Malignant Tumors of Bone, Cancer of the Eye, Hodgkin's Diseases, Sarcomas of Soft Tissues, and Leukemia (Chapter XX, pages 1058-1078). There is a good authors' index and an equally good subject index. The sections on "Tumors of The Thyroid Gland" (Chapter VIII, pages 464-480), "Tumors of the Liver" (pages 663-674), "Tumors of the Pancreas" (pages 644-663), "Cancer of the Gallbladder" (pages 674-681) and "Tumors of the Suprarenal Gland" (Chapter XIII, pages 777-796) while brief, are ample for most students and busy surgeons and clinicians.

For the gastroenterologists, the sections on the "Upper Digestive Tract", and the "Digestive Tract" (Chapter X, pages 492-693) will be most informative and instructive. These sections alone, for the gastroenterologists and clinicians make this book a "must", to be kept on the desk for quick and frequent reference.

In later editions, perhaps, there will no doubt be included more information about newer developments in therapy of this great killer of men.

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MEDICAL AND PHYSICAL DIAGNOSIS: INTERPRETATION OF FINDINGS. Samuel A. Lowenberg, M.D., F.A.C.P., Clinical Professor of Medicine, Jefferson Medical College; Assistant Visiting Physician, Northern Liberties Hospital, etc. 1181 pages, with 716 illustrations, 39 in color. Seventh Edition, F. A. Davis Company, Philadelphia, 1948. Price $12.00.

The seventh edition of this excellent book on Medical and Physical Diagnosis has been brought up to date. The book is a popular one as is evidenced by seven editions of the work. The author is an experienced teacher and clinician and the result of his extensive experience, and great interest in the medical students and the general practitioners, has been this very practical book on medical diagnosis. This new edition with corrections, and additions of much new material will be a welcome addition to the medical library of all practicing physicians and medical students. This textbook is enthusiastically recommended as a good practical book on medical and physical diagnosis. The descriptions of signs and symptoms of diseases, the meaning of many of the more modern laboratory tests, and the interpretation of the many newer physical signs, and the diagnostic problems related to the many syndromes described, are lucidly and concisely given by the author.

Most of the illustrations are quite good. The paper is of excellent quality. The two column arrangement of the pages, gives much information and allows for easy reading. In future revisions or reprints there might be included more references of importance to the rapidly growing amount of medical literature. Both the author and the publishers are to be commended and congratulated upon a "job well done"!

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PERIPHERAL VASCULAR DISEASES. David W. Kramer, M.D., F.A.C.P., Associate Professor of Medicine, Jefferson Medical College; Assistant Physician, Jefferson Hospital; Visiting Physician, Philadelphia General Hospital, etc. 630 pages, with 157 illustrations, 25 in color. F. A. Davis Company, Philadelphia, 1948. Price $8.00.

The author states that: "The purpose of this book is to furnish general practitioners, specialists, and students with modern information on the diagnosis and treatment of peripheral vascular disorders."

This textbook, written by an experienced clinician and one particularly interested for many years, in the management of cases of diabetes and the various complications, and of cases of various types of vascular disease, is a work that readily lends itself for study by the busy practitioner, the specialists, and the medical student.

The author gives careful and very concise consideration to symptoms, signs and tests; to acute and chronic vascular disorders, inflammatory and noninflammatory conditions, vasospastic disorders, gangrene, chronic leg ulcers, disorders of veins, anticoagulants and antibiotics, and disorders of the lymphatic system (lymphedema).

The author gives detailed information for the treatment of these conditions based chiefly on his personal experience of thirty years both as clinician and teacher.

This is one of the best books on the subject, and is recommended by the reviewer, as a desk copy for all medical practitioners.

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VIRUS DISEASES OF MAN. C. E. Van Rooyen, M.D., D.Sc, M.R.C.P., Professor of Virus Infections, University of Toronto, formerly Fellow, and Lecturer in Bacteriology, University of Edinburgh and A. J. Rhodes, M.D., F.R.C.P., Associate Professor of Virus Infections, University of Toronto, Consultant in Virus Infections, Hospital for Sick Children, Toronto, formerly Lecturer in Bacteriology, University of Edinburgh and University of London. 1202 pages. Thomas Nelson & Sons, New York, N. Y., 1948. Price $20.00.

In view of the great increase of our recent knowledge of virus diseases, diagnosis and treatment and, because of greater interest now, in the study of virus infections this second edition (1948) of

the best one-volume text on "Virus Diseases of Man" available, should be on the "must" list of all medical and hospital libraries and, a readily available copy on the desk of every physician interested in virus diseases.

The publishers, and the authors, are deserving of the thanks of the profession for the publication of such an excellent contribution to the study of virus diseases.

Rickettsial diseases, and viruses peculiar to animals or plants are not discussed in this work of 1202 pages.

"Virus diseases now occupy a major position in the ecology of man" (and animals) that this study of the environment and life history of these organisms (viruses), has become a subject of great importance, and, so this new edition, by two leading authorities, will certainly be of great help to all physicians and research workers in this field. In a brief book review it is impossible to touch upon all the important and valuable chapters contained between the covers of this outstanding work.

Suffice it to say, that this book can be enthusiastically recommended as a reference book, and as a most reliable text for careful study. "Technique" in Section I, is adequately and informatively discussed in thirteen chapters of 144 pages. "Diseases of the Skin and Mucous Membranes" in Section 2—and "Infective Fevers of Virus Origin" in Section 3, are discussed in twenty-two chapters of 284 pages. Herpes, measles, smallpox, alastrim, cowpox, mumps, chickenpox, postvaccinal encephalitis, vaccination and variolavaccinia virus are particularly well discussed.

Foot and mouth disease in man, stomatitis and diarrhea of infants, molluscum contagiosum, shingles, and verrucae (warts) are sufficiently covered.

In later chapters many of the other important diseases of the pneumonitis-psittacosis, L G I group, arthropod spread and other tropical infections, yellow fever, dengue fever, rift valley fever, sandfly fever, colorado tick fever, etc. are expertly presented.

The common cold and influenza are discussed in 141 pages (Chapter LII-LXIII), in Section 5.

The authors also present authoritatively and clearly, virus infections of the eye, including epidemic keratoconjunctivitis, trachoma and inclusive conjunctivitis. Rabies and pseudorabies or Aujeszky's disease, the poliomyelitis group of virus infections, virus menigitis, encephalomyelitis; St. Louis and Japanese type of encephalitis; the equine encephalomyelitis group of viruses, and, in the last section, infective hepatitis and homologous serum jaundice, are all satisfactorily and adequately presented. The authors are to be particularly complimented upon the very complete and exhaustive bibliographies—with thousands of references—included in this volume. These references usually follow each Chapter. One need only examine the references (Chapters XXVI-XXXV) on pages 404-429, following "postvaccinal encephalitis", the references listed on pages 758-762, on pages 783-791, on pages 887-906, to realize the amount of effort, time and labor, put into the production of this text.

The reviewer knows of no other single volume on this subject which even approaches this van Rooyen-Rhodes mag. opus!

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ENDOCRINOLOGY OF NEOPLASTIC DISEASES. A SYMPOSIUM BY EIGHTEEN AUTHORS. Gray H. Twombly, M.D. and George T. Pack, M.D. 392 pages. Oxford University Press, New York, 1947. Price $11.00.

This unusual volume on the endocrinology of neoplastic diseases, consists of a symposium, of an introduction by Twombly and Pack the editors, and sixteen contributions by leading authorities, on endocrinologic problems concerned with various neoplastic diseases.

Gardner, of New Haven, discusses tumors in animals receiving steroid hormones in the opening Chapter. Estrogens and androgens are considered, and a closing discussion on "Interpretation" of some of the material presented clarifies much of the recorded information.

Hans Selye adequately and expertly presents a survey of the experimental medical literature concerned with the role of the pitutiary in tumorigenesis in Chapter II (17 pages).

The endocrine effects of pituitary tumors is covered by William J. German, of Yale with several illustrations of historical interest—including Marie's acromegalic woman (1886), Babinski's hypopituitarism in a girl (1900).

Frohlich's syndrome in a boy (1901), Levi's (Lorain-Levi type) hypopituitarism in a girl (1908), Gilford's progeria in a boy (1897) and Keith's skull of the Irish giant O'Brien (1911) who died in 1783. He omits Simmond's case (1914) of "Simmond's disease" and Cushing's (1912) case of basophilism, although Jakob Erdheim, of Vienna described (1903) two cases of basophilic adenoma, and Cushing's report (1912), are mentioned by the author.

One of the informative chapters is contributed by Emil Novak, noted Baltimore gynecologist—on "Ovarian Tumors with Sex Hormone Function" (Chapter IV).

Howard C. Taylor, Jr. of New York discusses the endocrine factors in the origin of tumors of the uterus. Other contributors to this unusual volume are: Nathanson (Boston), Farrow (New York),

Moore (Saint Louis), Dean and Woodward, and Twombly (New York), Kenyon (Chicago); Cahill of New York, who discusses "Hormonal Tumors of the Adrenal" (Chapter XII) in 37 pages and is one of the best contributions in this symposium—; Jacob Lerman (Boston), Oliver Cope (Boston), and Allen O. Whipple (New York) on "Hyperinsulinism in Relation to Pancreatic Tumors"—presents his subject in the expert manner expected of one who has had such extensive experience in this field as Professor Whipple. The closing Chapter (XVI) is by Leo M. Davidoff noted New York neurosurgeon, who discusses "The Endocrinologic Aspects of Tumors of the Pineal Gland". Davidoff refers to Galen's knowledge in the second century, of the pineal gland, and admits that the mystery of the pineal gland still remains unsolved—even its glandular nature is still debatable!

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PRACTICAL BACTERIOLOGY, HEMATOLOGY AND PARASITOLOGY. E. R. Stitt, M.D., Ph.M., Sc.D., LL.D., Surgeon General, U. S. Navy (retired); Paul W. Clough, M.D., Physician in Charge, Johns Hopkins Hospital; Sara E. Branham, M.D., Ph.D., Sc.D., Senior Bacteriologist, National Institute of Health. Tenth Edition, 991 pp. (illustrated). The Blakiston Company, Philadelphia and Toronto. 1948. Price $10.00.

This is an indispensable volume for the pathologist and the diagnostician. The standing of its editors and of their contributors and collaborators lends it the weight of authority, and the capable handling of the vast amount of material makes it readily available for reference and utilization. The title of the book accurately indicates its scope; in fact, it renders more than the service it promises, for chapters such as the one on vitamins as food factors add to its value. The new antibiotics, sulfonamides and quinine succedanea are described, and this prompts the suggestion that the next edition of the work might well be rounded out by the inclusion of the antiseptics and fungicides, so as to make an even 1,000 pages.

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*Rafsky, H. and Krieger, C. I., The Treatment of Intestinal Diseases with Solutions of Water-Soluble Chlorophyll, (a preliminary report). Rev. Gastroenterology 15:549, 1948.

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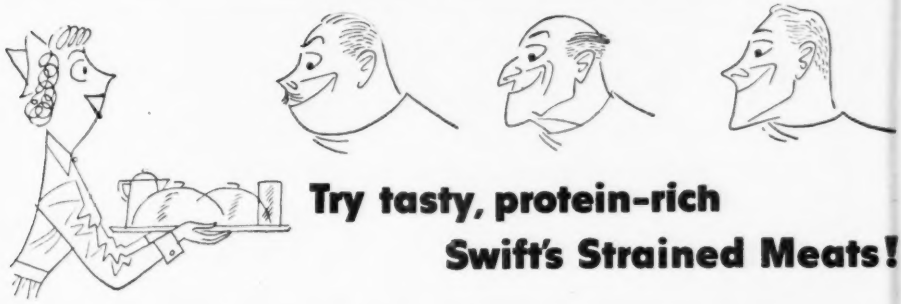

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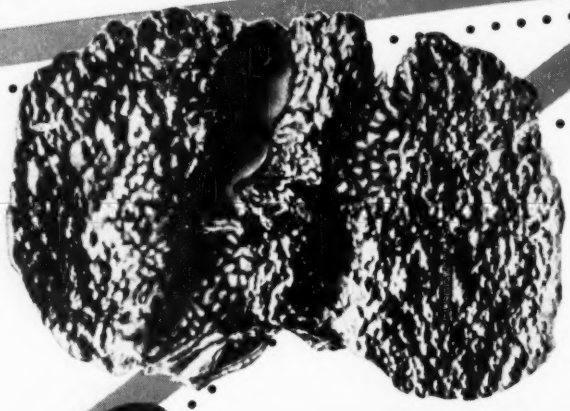

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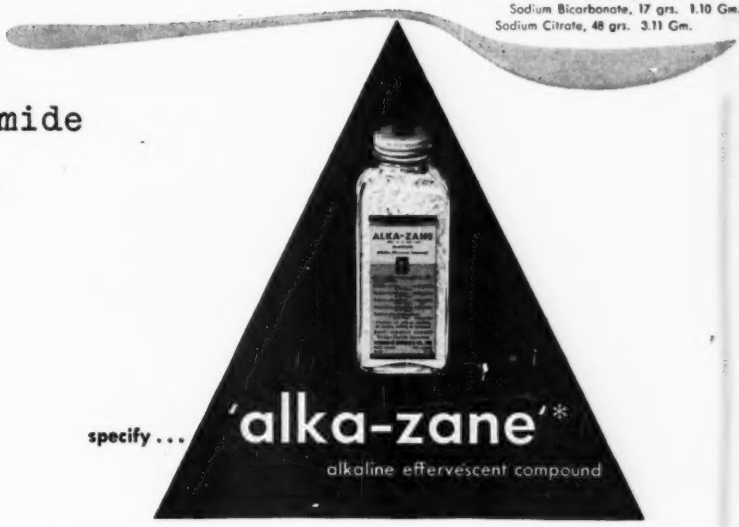


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